Clinical Medicine

Original Articles for July, 1958

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1. Meprobamate is more widely prescribed than any other tranquilizer. Source: Independent research organization; name on request.
2. Baird, H. W., III: A comparison of Meprospan (sustained action meprobamate capsule) with other tranquilizing and relaxing agents in children. Submitted for publication, 1958.

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GUEST EDITORIAL

X-Rays Are Good for People

The use of x-rays in diagnosis and treatment must be tempered by the same good judgment that dictates other therapy

ANTOLIN RAVENTOS, M.D., *Philadelphia, Pennsylvania*

Lately, there has been a generous supply of reports concerning the harmful effects of radiation. The National Research Council and the British Medical Research Council have published reviews of the subject. There has been much comment in the newspapers and magazines, on the radio, and even in the regular medical journals. At times some of us have questioned the assurance with which quantitative estimates of the hazard have been made and also whether some publications have been premature. We can rightly feel confused when one group of distinguished scientists tells us that radiologists suffer five years' shortening of life in comparison with other physicians who are not exposed to radiation, and another distinguished scientist interprets essentially the same data as indicating that radiologists may have a slightly *longer* life span than other physicians. Such contradictions indicate that our knowledge of the quantitative aspects of the hazard is still crude. Nevertheless, there seems to be no doubt that ionizing radiation even in small quantities can be harmful to tissues; in short, x-rays are bad for people.

At the same time, those of us engaged in the practice of clinical medicine know that x-rays are good for people, when skillfully used in medical diagnosis and treatment. How helpless we would feel *without* x-rays in many cases, for example, the differ-

ential diagnosis of chronic abdominal pain, of hematuria, or of persistent cough, to name just a few. Coller has written eloquently of the debt of surgery to roentgenology. Before the introduction of x-ray in 1896, he observed that the few surgical operations performed were for lesions "that would have been easily diagnosed by Hippocrates." Stone calls attention to the tremendous reduction in the tuberculosis death rate since 1900; most physicians would agree that diagnostic x-rays have played an important part in this achievement. Few of us, should we sustain a fracture, would feel that it was being treated properly unless x-ray was used to determine the number and position of the fragments, the alignment after reduction, and the state of healing before weight-bearing was resumed. Radiation therapy is consistently successful in curing some cancers and highly effective in relieving suffering in many forms of cancer at present incurable. Radioactive isotopes, which emit radiations essentially similar to x-rays, are also of established value in clinical medicine now.

USE OF X-RAYS ESSENTIAL

It is obvious that we must continue to use radiation if we are to maintain and improve the high standards that our medical practice has already attained. The *manner* in which we use radiation, however, must be tempered by a knowledge of its possible harmful effects. This is far from being a unique situation for us; nearly everything we do in medicine can at times be harmful. Some of the most innocuous medicines used have, on occasion, been responsible for serious anaphylactoid reactions in patients. Whenever we write a prescription, or perform any procedure at all upon a patient, the awareness of the possible dangers is a product of our training and experience. Indeed, it may sometimes be the most important professional service we have to offer our patients, for our knowledge of the inherent hazards of each procedure provides a basis for our judgment of what should be done and how to do it most safely.

Our consciousness of the hazards of radiation should sometimes lead us to advise against the use of x-rays. We should not permit any person to be exposed to even small doses of radiation without adequate indication. As we abhor the indiscriminate use of medicines, so we must oppose the use of x-rays when they are not really needed.

REDUCTION OF RADIATION DOSE

The high cost of medical radiation is an effective deterrent to its overutilization, however. We doubt that many *unnecessary* procedures are done. As doctors we cannot expect to reduce the exposure of our population appreciably simply by avoiding radiologic procedures, unless our standards of medical care are to suffer. A much more fruitful endeavor appears to lie in the fuller use of known methods for reducing the radiation dose in the procedures now being done. In x-ray diagnosis, for example, the use of proper cones and filters, of full dark-adaptation before fluoroscopy, and of modern equipment regularly tested for safety can greatly reduce the radiation exposure of critical organs without detracting from the clinical value of an examination. It seems quite likely that increased attention to proper technique can permit us to decrease the radiation exposure of our population substantially even while the actual utilization of radiation in medicine is in-

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creasing. The ways and means of using x-rays with maximum safety are described in a booklet prepared under the auspices of the American College of Radiology. The nature of radiation hazards to man are also briefly but comprehensively summarized in this booklet, which is being made available to every physician and dentist.

PROTECTION FROM RADIATION

In addition to being the custodians of our patients' safety with regard to medical radiation exposure, we have a responsibility to ourselves and our co-workers. Radiation exposure is an occupational hazard of every physician who uses x-rays, radium, or radioactive isotopes, and of his nurses, technicians, and assistants as well. We all know about the pioneer users of x-rays, who in many instances were crippled, or even died, as a result of the radiation injuries they accumulated unknowingly. We expect that modern knowledge of radiation protection will prevent us from sustaining any serious radiation injuries, but we must remember that knowledge of protection techniques is valueless unless it is applied. One cannot see or feel the damage while it is being done; for the most part, the effects of injudicious occupational exposure do not make their appearance until years after the events. Thus the common argument that "I've been doing this for years and it has never hurt me yet" reminds us of a story told in a recent novel of a man who, having fallen from a tall building, called out as he passed some people in a window about halfway down for them not to worry because he was all right so far.

There is little that is really new about the radiation safety problem except the wider public awareness of it. It has been with us since we started using x-rays medically, and it is not likely to diminish in importance. We have dealt with it and must continue to deal with it just as we do the many other iatrogenic dangers—with information, perspective, and common sense. The individual patient is no better equipped to decide when he should or should not be exposed to medical radiation than he is to prescribe his own treatment; he must rely upon the balanced judgment of his physicians, whose advice is founded upon the entire body of scientific medical knowledge. Part of the tradition of our profession is the obligation to lifelong study in order to keep abreast of scientific advances. We have studied radiation and found ways in which it is an invaluable aid to us. We shall almost certainly find still more ways in the future. At the same time, we have found hazards in radiation exposure. It is our job to know and appreciate these complex and subtle hazards; we must be able to view them in their proper proportions, we must know when and for whom they are most important, and we must use every practical technique to minimize exposure to our patients, our helpers, and ourselves. Only then can we be sure that, in measure far outweighing the potential harm, x-rays are good for people.

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ORIGINAL ARTICLE

Relief of Allergic Symptoms With Tranquilizers In Combination With Other Drugs

Advantages and limitations of tranquilizers when they are used for symptomatic relief and to help allay emotional tensions of allergic patients

BEN C. EISENBERG, M.D.,* *Huntington Park, California*

In the care of allergic patients there is no substitute for a comprehensive history, careful examination, especially of the nose, throat and chest, indicated skin testing, and specific allergy management using proper dosage of significant antigenic materials. This time-tested approach is responsible for the improvement of 75 per cent of those suffering from allergic diseases. Instead of replacing the usual type of allergy treatment, the antihistamines, ACTH, corticosteroids, and now the tranquilizers,[1] have become useful aids for the temporary relief of symptoms while the problem is attacked from an etiologic standpoint.

In asthma, as in all other diseases, it is important to treat the whole patient. In order to do this we must get to know him. What is his general attitude? What are his aims and ambitions? Is he happy in his job or lot in life? How about his family relations—past and present? Does he evidence undue anxiety, hostility or neurotic behavior? Is he mentally depressed? In the case of a child patient, what are the parents like? During skin-testing, or as the patient returns, we are afforded an opportu-

* Medical Department, School of Medicine, University of Southern California, and Allergy Clinic, Los Angeles County General Hospital.

1. Eisenberg, B. C., *J.A.M.A.*, 163:934,1957.

nity to observe and to learn much of value.

Physicians caring for allergic patients should appear unhurried, and encourage the patient to talk freely. The first interview and examination is most important in showing your interest in the patient and in his case. In the cases of children and teen-agers, considerable effort must be made to make them feel the doctor is sympathetic. A physician must often serve as a kind, though firm, parent-substitute for his patients. Use of fancy psychiatric terms, or reference to "psychosomatic," should be rare.

UNUSUAL ALLERGIES

A few of the more vague and unusual types of symptom-complexes which often yield to good allergy management are:

1. Periodic, or frequent, upper respiratory infections, recurring every two to six weeks, with or without fever, and accompanied, usually, by nasal stuffiness, rhinorrhea, and a troublesome cough.
2. Recurrent canker sores of mouth and pharynx.
3. Periodic herpes simplex involving the face or other parts of the body.
4. Unexplained, frequent attacks of gastrointestinal difficulty—colic, nausea and vomiting, diarrhea.
5. Urinary disorders, such as dysuria and frequency, without known organic cause.
6. Recurring headaches, including migraine, where CNS and other causes have been eliminated.

TREATMENT OF BRONCHIAL ASTHMA

Symptomatic treatment of bronchial asthma depends on the severity and duration of attacks, and on whether any complications exist. Look for any of the following when the usual measures fail to bring about relief:

1. Undue exposure to animal danders, pollens, and fertilizer, grain-mill, castor bean or other dust.
2. Respiratory infection, sometimes in the absence of fever and leucocytosis. Here, the physician should look for colored, purulent sputum, and listen carefully for crackling rales, apart from the wheezy, asthmatic breath sounds.
3. Dehydration, and mucus plugging of bronchioles. This usually is the result of three factors: (a) the patient is too tired to eat or drink, and he is too busy trying to breathe; (b) most of the drugs used in asthma either dry out the mucous membranes, promote diuresis, or over-sedate the patient and reduce his desire for fluids; (c) labored respirations, like any other physical effort, is attended by excessive perspiration and additional fluid loss through the lungs.
4. Pulmonary diseases such as emphysema, atelectasis, pneumothorax, rupture of a bleb or cyst, tumor, TB., pneumonia, or bronchiectasis.
5. Heart failure — left ventricular, or cor pulmonale.
6. Anaphylactoid reaction to serums, vaccines, insect bites, antibiotics, or other drugs, especially aspirin.
7. Exposure to chemical fumes, as ammonia, chlorine, smoke, strong perfumes or cooking odors.
8. Excessive physical exertion, or even paroxysms of laughing or coughing.
9. Psychogenic factors, as acute or chronic anxiety, mental depression, or other disturbances resulting from

difficult home, school, or job situations, or repressed hostility and resentment toward a parent, spouse, sibling or boss.

10. Adrenal insufficiency following withdrawal of ACTH or corticosteroid medication.

Each of the items in these categories dictates its own therapy. Certain general principles hold, however, for all cases of intractable asthma not responding to conventional methods of treatment.

FLUIDS

Ample fluids must be given, orally or parenterally, to prevent or relieve dehydration. Two or three liters may be required daily, via the intravenous route, using five per cent glucose in distilled water, 60 to 90 drops per minute flow. Experience has taught that neither ACTH nor aminophylline is of much aid when added directly to the intravenous solution. Both place an additional strain on the body defense mechanism, and aminophylline given in this manner promotes nausea and causes loss of fluid through the kidneys faster than one can pour it into the vein. Saturated KI by mouth (15 drops t.i.d.) or iodine tablets[2] (one t.i.d.) helps liquefy tenacious sputum. It is best to stop all medications, especially adrenalin and aminophylline, if the patient no longer responds to them.

ANTIBIOTICS

Since some infection usually supervenes in bronchi obstructed for 36 to 48 hours, an antibiotic, preferably via the oral route, should be given for a few days, longer in cases of obvious respiratory infection. Penicillin may be used intramuscularly, provided the patient is not allergic to this drug. Erythromycin appears least likely to disturb the intestinal flora, or precipitate skin or other allergic reactions.

NARCOTICS AND SEDATIVES

Many physicians erroneously equate the restless, wheezy, grunting asthmatic with the post-operative surgical case in distress, and prescribe enough codeine or phenobarbital to quiet either type of patient. Let us remember it is better to have a moaning, groaning asthmatic than a silent one with a seriously depressed respiratory center, thus making slim his chances for recovery. A combination of secobarbital sodium and amobarbital sodium[3] grains 1½, or butibarbital sodium,[4] in similar dosage, given at bed-time, usually provides ample sedative effect, and one need rarely use anything stronger.

TRANQUILIZERS

Ataractic drugs have largely replaced sedatives such as the barbiturates. For the ambulatory asthmatic, whose symptoms may be aggravated by acute or chronic anxiety, one of the following may be selected:

1. Reserpine[5] may be given in daily doses of 1 to 3 mg. for a few days, then reduced according to response, or by intramuscular injection, 2.5 to 5 mg. per day, continuing afterward with the oral preparation. For the first few nights a mild barbiturate should be given for sleep. It may become necessary to change to another type of medication because of appearance of side-effects,

2. *Organidin*, Henry K. Wampole & Co., Inc., Stamford, Conn.

3. *Tuinal*, Eli Lilly & Co., Indianapolis.
4. *Butisol* Sodium, McNeil Laboratories, Inc., Philadelphia.
5. *Serpasil*, Ciba Pharmaceutical Products, Summit, N. J.

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such as nasal congestion, gastric distress, mental depression, or increasing drowsiness and fatigue.

2. The injectible form of promazine[6] 25 to 50 mg. intramuscularly, two or three times daily, is used in office or hospital. The use of chlorpromazine[7] may be dangerous in asthma. Rarely should more than 25 mg. be given by injection and not to patients already sedated. Prochlorperazine[8] is effective in dosages of 5 to 10 mg., three times daily. Mild but transient dizziness or drowsiness occur in some instances.

3. Meprobamate[9] acts primarily as an anticonvulsant and muscle relaxant. It also lessens fear, hostility, and aggressiveness. It is especially effective in tension headache and anxiety states. However, in 14 per cent it causes some sort of toxic or allergic reaction, even anaphylactoid shock. The usual dose is 400 mg., three or four times daily.

4. Hydroxyzine HCl[10] acts as a mild anticonvulsant, has an analgesic effect, demonstrates atropine-like qualities, and neutralizes the emetic effect of apomorphine. It will also lower hypertension due to anxiety states, but not that caused by organic disease. Recent experiments have shown this drug to have antihistaminic, anti-serotonin and anticholinergic effects.[11] Aside from occasional headache or drowsiness, it is virtually non-toxic. In well over 200 cases, it was found to be effective in alleviating anxiety-induced allergic symptoms. It is especially valuable in helping to calm the "hyperkinetic" child. It has also proved an aid in stopping enuresis. It is given in dosage of 10 to 30 mg. three or four times a day. It is particularly helpful in urticaria cases, and may be combined with other anti-allergy drugs.

5. A chlorpromazine derivative[12] is comparable in effect to prochlorperazine, being a highly useful anti-emetic. It affords good tranquilizing action, and may be administered to children in small doses. Adults are usually given 4 to 8 mg., three or four times daily.

Moderately severe asthma, or status asthmaticus, requires hospitalization, preferably in a dust-free room, devoid of possible allergens such as feathers, dusty blankets, heavy cooking or perfume odors, flowers, bath powders, or insect sprays. Treatment consists, for the most part, of stopping ineffective medication, such as antihistamines, aminophylline, ephedrine and adrenalin; hydrating the patient as outlined above; giving antibiotics if infection is suspected; judicious use of tranquilizers, and steroid hormones.

ADRENOCORTICOSTEROIDS AND ACTH

In most cases requiring this type of treatment, short courses of from one to three weeks usually suffice. Because ACTH is slow in its effects, it is preferable to use the oral medications, prednisone or prednisolone —20 to 40 mg. at once, repeating this same amount, if necessary, the following day, following with a maintenance dose of 5 or 10 mg. each night for several nights. This type of therapy causes much less depression of adrenal activity than divided-dose schedules maintained for a

6. *Sparine*, Wyeth Laboratories, Philadelphia.
7. *Thorazine*, Smith, Kline and French Laboratories, Philadelphia.
8. *Compazine*, Smith, Kline and French Laboratories, Philadelphia.
9. *Miltown*, Wallace Laboratories, New Brunswick, N. J.
10. *Atarax*, J. B. Roerig & Co., New York.
11. Feinberg, A. R. et al, *Hydroxyzine as an Antiallergic Drug* (to be published).
12. *Trilafon*, Schering Corporation, Bloomfield, N. J.

longer period. Children apparently tolerate similar amounts well, and usually show rapid recovery of adrenal function when the steroid drugs are stopped.

Patients requiring prolonged steroid medication should be maintained at the lowest possible level—5 to 15 mg. in single dose every other day—for fair relief of symptoms. Watch for signs of infection or gastric irritation, and cover with appropriate treatment. Watch, also, for osteoporosis and negative nitrogen balance, and, in children, keep check on thyroid activity, growth and development. In the cases of patients who show little benefit from more than 15 mg. daily, and require considerable quantities of additional medicines (adrenalin, ephedrine, isuprel, aminophylline, etc.), the steroids should be discontinued and the condition appraised from all angles.

Many times quick relief of asthmatic attacks is achieved by using adrenalin along with an injectible tranquilizer, plus a solution of diphemanil methylsulfate.[13] This combination works especially well in children with asthma accompanied by a great deal of nausea and vomiting. The following dosage is well tolerated by adults, lesser amounts by children:

a. Epinephrine (1-1000) — 0.3 cc.
Prantal (25 mg./cc) — 0.4 cc.
Sparine (50 mg./cc.) — 0.5 cc.
b. Epinephrine (1-1000) — 0.3 cc.
Prantal (25 mg./cc) — 0.4 cc.
Serpasil (2.5 mg./cc) — 0.5 cc.

In addition, hydroxyzine may be given, 10 to 25 mg. t.i.d., for further tranquilization.

URTICARIA AND ANGIOEDEMA

It is rarely found necessary to administer epinephrine or ephedrine by injection for this condition. While the patient may obtain temporary relief from such drugs, the skin manifestations recur with much greater intensity, suggesting a temporary damming up of certain chemical substances responsible for the whealing reaction. When such a process threatens the laryngo-pharyngeal tissues, prompt treatment with adrenalin, antihistaminics and steroids is demanded with a stand-by tracheotomist handy.

ACUTE URTICARIA

For acute cases, antihistaminics may be given by intramuscular injection initially, followed by oral medication, and one of the following, also by intramuscular injection: *Prantal* and *Sparine*—0.5 cc. of each; or *Prantal* and *Serpasil*—0.5 cc. of each. Hydroxyzine, 60 to 100 mg. daily, in divided dosage, is a valuable adjunct in the treatment of urticaria, while trying to find the cause, and steroid therapy is begun, if necessary, to bring about quicker termination of the attack.

CHRONIC URTICARIA

Chronic, recurrent urticaria requires intensive investigation. Food allergy, drug allergy, infection, and psychogenic factors must be considered. In the meantime, symptomatic relief may be afforded by hydroxyzine, which appears to be the best single medicine for chronic urticaria, and occasional use of ephedrine-aminophylline combinations or *Prantal-Sparine* injection. It is also important in these cases to attempt to pinpoint one or more irritating life-situations which may be triggering the urticarial response. Above all avoid the use of other drugs, including vi-

13. *Prantal*, Schering Corporation, Bloomfield, N. J.

tamins, androgens, estrogens, thyroid, amphetamines, vaccines, serums and antibiotics, as these may cause the urticaria of such patients. Should an antibiotic be needed, erythromycin is less likely to aggravate symptoms of allergy.

CONCLUSION

Used in the manner outlined, tranquilizers can afford allergic patients additional symptomatic relief, through allaying emotional tensions. These drugs block certain adverse neurogenic reflexes, and, in addition, exert favorable antihistaminic, anti-anaphylactic, anti-serotonin and anti-cholinergic actions. As an antiallergic, hydroxyzine has been found to be the most potent of this class of drugs, especially in chronic urticaria—without producing too much sedation. Once symptomatic control is fairly well established, the condition should be studied and treated from the etiologic standpoint. This implies a complete allergic investigation and a psychosomatic approach to the problem.◄

Cancer-Cell Seeding of Operative Wounds

The treatment of most carcinomas is directed toward the destruction of the tumor tissue, both at its site of origin and its areas of spread. The ineffectiveness of present cancer therapy is attested by the low survival rate. The important problem is to learn the reason for failure in the 60% to 70% of the cancer patients who die of their disease. In studying the few reports in which data are available, it is noted how frequently treatment fails because of inability to control the local disease in the area of surgery.

In the first 113 cases studied, cancer cells were demonstrated in 31 (positive results), and in an additional 16 cases, the cytologist could not be sure as to the nature of the cells and reported the washings as suspicious. The identification of malignant cells in wound washings did not present a difficult problem.

It is believed that, in at least some cases, local seeding can be demonstrated as a cause of treatment failure. If effective local chemotherapy can be accomplished at the time of primary surgery, an increase in our salvage rate should be accomplished. If effective chemotherapeutic agents are discovered, which can selectively destroy cancer cells that either become embedded in the wound, or break off and are free in the blood or lymph channels, effective cancer therapy will be available.

Smith, R. R. & Hilberg, A. W., *J. Maine M. A.*, 48:151-156,1957.

ORIGINAL ARTICLE

An Effective Medication in the Treatment of Premenstrual Tension

Well tolerated, with a minimum of side effects, this medication brought significant improvement to 85% of 70 test patients

ALBERT J. LEVINE, M.D., MORRIS FINKEL, M.D., IRVING M. FORMAN, M.D., and WILLIAM I. FISHBEIN, M.D., *Chicago, Illinois*

In recent years the syndrome of premenstrual tension has attracted considerable attention among physicians who have had the opportunity of observing its physical and psychological effects. The visible manifestations may not constitute a hazard to health, but the end-results may be some degree of personal maladjustment, disharmony in interpersonal relationships, and decreased earning capacity in those who depend upon employment.

Billig,[1] following a series of extensive observations in industrial plants employing 500 or more women, demonstrated from 36 to 43 absentee days and 62 days of decreased efficiency per month per 100 women, as the consequence of the need for extended relaxation or sedation during the premenstrual period. Premenstrual tension involves an average wage loss of $15,500 per year per 100 subjects.[2] It has been estimated that 36% of the women employees in industrial plants require medication during the premenstrual period.[3]

1. Billig, H. E., Jr., *Internat. Rec. Med. & G.P.C.*, 166:487-491,1953.
2. Billig, H. E. Jr., Unpublished data.
3. Bickers, W., & Woods, M., *Texas Rep. Biol. & Med.*, 9:406-419,1951.

Similar observations are recorded in this study. From the standpoint of industry, it would be most desirable to have a medication capable of controlling these complications of the menstrual cycle.

Although premenstrual tension manifests itself in various symptoms of pain and swelling of the breasts, abdominal bloating, backache, cramps, irritability, etc.,[4] the majority of these symptoms may be the result of a few underlying basic disturbances in normal physiology.

Weight gain is a frequent concomitant of premenstrual tension, often demonstrable in the form of clinical edema, and abrupt disappearance of this symptom is usually accompanied by a pronounced diuresis. Many investigators have theorized that the symptoms of premenstrual tension may be attributed to the retention of fluids and electrolytes.[5-8] In turn, the retention of fluid and electrolytes has been attributed to an imbalance of estrogen and progesterone in the circulating blood. A variety of explanations have been offered.[5,9-13]

The theory has been advanced that premenstrual-tension hypoglycemia may serve as the direct cause for the frequent weakness, nervousness, and tendency toward poor coordination and that an autonomic imbalance, with overactivity of the parasympathetic nervous system, plays a predominant role in the production of these symptoms.[13]

A medication that combines a number of ingredients designed to counteract not only the fluid retention, but to offset the other disturbances, particularly those referable to the autonomic imbalance and the hypoglycemia is available as *Pre-Mens.**

This medication was used in a study in a series of women taken from our industrial practice.

METHODS OF STUDY

Ninety women, aged 20 to 40 years, all displaying fairly regular menstrual cycles and symptoms of premenstrual tension were selected for the study. In addition, 61 of these patients complained of dysmenorrhea.

After comprehensive case histories, the patients were observed for a period of a few months to derive a characteristic behavior pattern. For the next six months, each patient was treated with one of two medications, and the effect of each was observed and recorded.

During this test period, the preparation was administered to 70 patients, while 20 were treated with a placebo as a control. During each cycle of administration, the patients received two tablets of *Pre-Mens* three times daily, starting ten days before the menses, and continued daily until the onset of the period.

The effect of the medication was assessed by two methods.

Each patient was examined at

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5. Frank, R. T., *Arch. Neurol. & Psychiat.*, 26: 1053-1057,1931.
6. Thorn, G. W., et al., *Endocrinology*, 22:155-163, 1938.
7. Greenhill, J. P., & Freed, S. C., *J.A.M.A.*, 117: 504-506,1941.
8. Hurxthal, L. M., & Musulin, N., Clinical Endocrinology, Philadelphia, W. B. Saunders & Co., 1953.
9. Israel, S. L., *J.A.M.A.*, 110:1721-1723,1938.
10. Biskind, M. S., *J. Clin. Endocrinol.*, 3:227-234, 1943.
11. Morton, J. H., *Am. J. Obst. & Gynec.*, 60:343-352,1950.
12. Greene, R., & Dalton, K., *Brit. M.J.*, 1:1007-1014, 1953.
13. Morton, J. H., et al., *Am. J. Obst. & Gynec.*, 65:1182-1191,1953.

*Purdue Frederick Co., New York. Each tablet contains: Ammonium chloride, 330 mg; homatropine methylbromide, 0.5 mg; caffeine alkaloid, 33 mg; thiamine hydrochloride, 2.0 mg; riboflavin, 1.0 mg; pyridoxine, 0.5 mg; calcium pantothenate, 1.0 mg; niacinamide, 5.0 mg.

periodic intervals throughout the course of the study. The industrial nurse also recorded observations on these patients.

Each patient was furnished with a diary, in which was recorded the presence and degree of severity of symptoms, as well as body weight gain under standardized conditions each day.

At the end of the six-month period the results were analyzed.

RESULTS

Seventy patients received the tablets each month during the six-month study. Of these, 49, or 70 per cent, obtained excellent relief from their symptoms; 15 per cent obtained good results, and 15 per cent experienced little or no relief. The medication proved effective in suppressing symptoms of premenstrual tension in 85 per cent of the patients. Patients reported freedom from symptoms of mastodynia, abdominal bloating, etc., and relief from anxiety, irritability, depression, etc. For months before administration the average weight gain during the premenstrual week was 3.9 pounds but during administration this average weight gain was decreased to 1.2 pounds. There was an increase in the amount of urine voided during the period of ingestion of the drug. The increased frequency reported by the majority of patients was unsolicited, and was more in the nature of a complaint.

Of the 20 patients who received the placebo, 6 reported some relief from symptoms during the cycles when they received *Pre-Mens.* Fourteen reported no relief.

MINIMAL SIDE EFFECTS

The medication was well tolerated by the patients. Only four (six per cent) reported any side effects. Three of these were in the form of nausea and one as a papular rash. Nausea is not an infrequent symptom of premenstrual tension.

DISCUSSION

In this series of patients, the medication greatly improved both the somatic and "mental" symptoms in the majority of patients treated. It was found to be an effective treatment in preventing painful swelling of the breasts, adbominal bloating, headache, and nervousness. It was somewhat less effective in counteracting depression, insomnia, and backache, but in these complaints relief was also noted. The medication appears to be an effective medication for the treatment of premenstrual tension. This confirms similar reports by other investigators.[4,13-15]

SUMMARY

Of 90 women from industrial plants with regular symptoms of premenstrual tension who were subjected to a study of the effect of *Pre-Mens,* 70 received the drug during each cycle of the six-month period; 20 received a placebo identical in appearance.

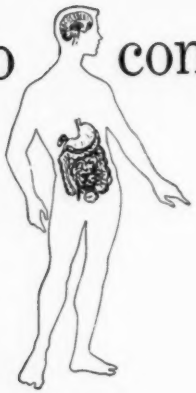
Of the 70 patients to whom it was administered, 60, or 85 per cent, obtained excellent to moderate relief. Only 10, or 15 per cent obtained little or no relief.

Patients receiving placebos failed to exhibit significant improvement in their premenstrual tension.

The medication was well tolerated by the patients with a minimum of side effects.◀

14. Greenblatt, R. B., *G.P.*, 11:66-68,1955.
15. Eichner, E., American Medical Association, Scientific Exhibit, Presented at the Section of General Practice, Chicago, 1956.

to control stress



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ORIGINAL ARTICLE

Operative Complications of Anorectal Surgery

The surgeon must be prepared to correct an adverse postoperative course. A plan for avoidance and correction of complications is presented

RAYMOND E. ANDERSON, M.D., M.S., F.A.C.S.,
McMinnville, Oregon

Operative procedures undertaken for the relief of benign anorectal disease are frequently followed by distressing and disabling complications. This accounts for the reluctance of people to undergo anorectal surgery, and their willingness to accept other methods of treatment. Failure to correct an adverse postoperative course in both its physical and emotional components produces a patient who is despondent, filled with misgivings, skeptical, and resentful at the outcome of his surgery.[1]

Postoperative complications are annoying or disabling to the patient and embarrassing to the surgeon. Evasion is futile and procrastination is inexcusable. Positive steps must be taken if the patient's confidence is to be restored. One or more of the following circumstances may be accepted as being a complication to benign anorectal surgery, when its presence retards normal recovery of the patient by altering his state of general well-being, or prevents restoration of a normal function to the anorectal mechanism:

1. Hemorrhage.
2. Excessive postoperative pain.
3. Infection.
4. Outlet stenosis.
5. Incontinence.
6. Mucocutaneous fistula.

1. Anderson, R. E., et al., J.A.M.A., 159:9-17,1955.

7. Alteration of mucocutaneous junction.
8. Pruritus.
9. Anal ulceration.
10. Fecal impaction.

HEMORRHAGE

Postoperative bleeding in significant amounts comes from either the skin margin, the external anal sphincter muscle, or above the mucocutaneous line (internal bleeding).

Skin Bleeding

Treatment of most benign anorectal lesions calls for the removal of enough skin to assure proper drainage and healing. This denuded area may ooze or bleed for some time. Prolonged or excessive hemorrhage from this area is readily controlled by dry pressure dressings, but if it is persistent, investigation of the blood clotting mechanism is warranted.

Bleeding from the Internal Sphincter

The inferior hemorrhoidal artery supplies the external anal sphincter with many small branches which may easily be incised during the course of an anorectal operation. The passage of bright red blood from the rectum at any time during the postoperative period calls for a thorough examination. A topical anesthetic jelly may be applied to the anal canal and an anoscope gently introduced so as to visualize the entire operative area. If one is unable to examine under this anesthesia, procaine solution (1%) is infiltrated into the skin and muscle until relaxation is obtained. When the bleeding vessel is found it is clamped and ligated with a No. 2 plain catgut. No other packing or hemostatic agent is used.

Internal Bleeding

The passage of large, dark blood clots with other signs of blood loss is evidence of hemorrhage above the mucocutaneous junction. Vigorous bleeding requires the transfusion of 500 cc. of whole blood and the placing of a pack into the lower rectum and anal canal. When such measures fail to stop the flow, the patient must be returned to the operating room, given a general anesthetic, and the bleeding vessel identified and suture ligated with No. 0 plain catgut. If a hematoma has developed, which may in some cases obliterate the open vessel, it is better to accurately place a larger, dumbbell type pack, than to attempt blind suture of the rectal wall. This pack is left in place 48 to 72 hours, then cautiously removed under heavy sedation. A low-residue diet is given for several days following this procedure.

To reduce the likelihood of postoperative bleeding, the ligation of hemorrhoidal veins at a point cephalad enough to obliterate the main channel is essential. A running, locking suture is the most efficient means of closing the collateral channels in the open hemorrhoidal bed. Arteries are always individually clamped and ligated. Before any knots or sutures are cut, the strands are relaxed in order to insure that the knot itself, rather than its tension, has controlled the bleeding. Inspection of the entire area as the final act of the operation will often save a return to the operating room within a few hours.

POSTOPERATIVE PAIN

This pain is often difficult to estimate, because of the inter-relation-

ship of functional and organic elements in its pathogenesis. The manifestation of extreme postoperative pain has often had its origin in the fear of cancer. Bedside psychotherapy may prove successful in patients who are apparently suffering agonizing postoperative pain.

Failure to do enough denuding at the mucocutaneous line results in edematous and congested tags of tissue, which are rich in nerve endings and interfere with drainage of the operative bed. Inflammation may rapidly develop, adding to the patient's discomfort. On the other hand, excessive denudation in the anal canal or outlet allows direct irritation of the very sensitive fibres of the external anal sphincter, constriction occurs and the vicious cycle of pain, spasm and improper healing begins.

Improperly placed sutures or ligatures which incorporate the fibres of the muscle bundle itself will also lead to trouble. Careful dissection of the muscle fibres prior to clamping is the only means of prevention.

Some surgeons still believe that a postoperative anal pack is a routine necessity for hemostasis. It does little or no good and is uncomfortable to the patient.

Infection and fecal impaction, common causes of pain, are discussed elsewhere in this paper.

Somatic innervation reaches only as far as the mucocutaneous line, so only a feeling of fullness, distension or congestion, and no severely painful sensations, will originate above this point. For those persons in whom edematous, swollen perianal skin is the basis for discomfort, the use of warm hypertonic saline packs or salt water Sitz baths serves best to relieve the congestion. When too much skin has been removed the liberal use of aqueous solution of Mercurochrome (1 or 2%), applied twice daily, acts as a soothing antiseptic and stimulates rapid epithelization of the defect. Topical anesthetic agents may be applied cautiously, but any irritation or maceration of the perianal skin demands their withdrawal. Sutures or ligatures that have penetrated into the sphincter muscle require a local anesthetic with removal through an anoscope.

Frequent postoperative digital dilatations of the anal canal, using liberal amounts of anesthetic jelly, help in breaking down adhesions and preventing the sealing of the skin edges, which in turn assures better healing, promotes drainage, and lessens spasm and irritability of the anal sphincter. The utilization of long-acting curare compounds will lessen muscle spasm. Local injection of the long-acting anesthetic compounds into and about the anal sphincter must be carried out with caution, the untoward effects following their use may be more distressing than the original condition. Superficial necrosis, deep abscess formation, local itching and urticaria, in addition to possible systemic reactions, are among the complications that develop.

INFECTION

By establishing free drainage of the traumatized and susceptible area at the time of surgery, potentially virulent bacteria, blood, serum and necrotic tissue are passed on out, and do no harm. Failure to make wide, radical incisions for the exit of these products is the most com-

mon cause of postoperative infection. Other factors include the inoculation of pathogenic organisms into the deeper tissue by the passage of sutures, examination or manipulation in the postoperative period with dirty gloves or instruments, and irritation, inflammation and direct invasion of the area by potent diarrhea-producing intestinal or respiratory bacteria. The majority of postoperative infections begin at the anal margin, in the posterior triangular space, or due to faulty surgical approximation at the mucocutaneous line. Chills, fever and malaise develop early and may be extreme, while the local reaction leads to pain, burning, pruritus and frequently to tenesmus and dysuria.[2]

Treatment consists of application of the principles used to combat infection wherever it may occur: rest, assurance, proper hydration, adequate vitamin intake, proper antibiotics or chemotherapy. Hot compresses help re-establish free drainage. Abscess formation requires incision at the anal margin or above the mucocutaneous junction. Examination or incision may be carried out under intravenous thiopental sodium. Frequent postoperative digital dilatations of the anal outlet are continued as the best means of re-establishing drainage.

OUTLET STENOSIS

This may result from removal of too much skin, leaving no bridge of epithelium between segments removed, or postoperative infection or inflammation at or below the anorectal junction. In either case the pathogenesis consists of deposition of fibrous tissue, which contracts to form a scar, which draws the anal outlet into a fixed and inelastic aperture.

Diagnosis is established by a careful digital examination of the anal canal. An extremely irritable external anal sphincter may necessitate anesthesia for evaluation of the degree of narrowing.

Frequent postoperative digital dilatations of the anal outlet will prevent too-rapid healing of the skin and junctional tissue, and thus allow a certain degree of epithelization to occur. Induration will be minimized. Stretching and massage aids in softening and relaxing the fibrous bands. In the event that contracture has already developed, several radial incisions are made deep enough to completely sever the fibrous ring, but never cutting the underlying fibers of the sphincter ani. No attempt should be made to dissect away a portion of the scar, nor should undermining or removal of wedge-like masses of tissue be undertaken—extra trauma leads only to increased hemorrhage and fibrosis.

The incisions should originate well above the zone of the scar and be continued in a caudal and peripheral direction far enough to insure proper drainage. The anal canal is dilated twice weekly for as long as eight to 10 weeks, and even then the anal orifice may remain at less than optimum caliber. If the patient is free of pain, however, and has established a fairly normal bowel habit, it is best to make no further attempts to repair the anal outlet. Divulsion of the anal canal as a remedy for anal outlet stricture is unsatisfactory. The submucosal hemorrhage so produced augments the fibrosis. Incision of the pectinate band in the

2. Anderson, R. E. & Witkowski, L. J., *Surgery*, 41:790-793,1957.

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*Biegeleisen, H. J.: Clinical Medicine; Oct., 1955

*Roberts, J. T.: Clinical Medicine; Nov., 1957

posterior midline will give relief to those people whose fibrosis is limited to this structure.

INCONTINENCE

With the possible exception of cancerophobia, the fear of incontinence of gas and feces is uppermost in the minds of persons facing anorectal surgery. Anal incontinence is most commonly the consequence of laceration of the sphincteric muscles at the time of surgery, with faulty healing of the incised or evulsed fibres. Various degrees of incontinence may also follow mechanical distortion of the anal canal, quite independent of muscle injury, as a consequence of faulty approximation of the mucocutaneous junction, development of mucocutaneous fistula, or the presence of scarring or stenosis of the outlet.

Although a tedious and painstaking undertaking, dissection of the frayed fibers from the scar tissue mass and a direct end-to-end approximation of viable muscle probably offers the greatest chance for restoration of sphincteric function. Over-correction of the defect should be the object, yet extreme caution must be exercised lest too much tissue be removed. Mattress sutures of absorbable surgical catgut serve well. Imbrication or reefing of the scarred or everted segments of the anal wall, especially in those cases in which the hiatus type of distortion is present, with a funnel-like deformity of the anal margin and prolapse of the mucosa may be necessary, especially in cases of long-standing incontinence.[3]

MUCOCUTANEOUS FISTULA

The tegumentary layers of the anal canal and perianal margin heal rapidly after surgical trauma, epithelization of denuded areas progresses at a faster rate than repair of the underlying tissues. A tunnel-like defect results, which lends itself readily to the formation of abscess tracts and fistulas. A mucocutaneous fistula, serving as the nidus for bacterial growth and inflammation, must be avoided if possible, or promptly eliminated when discovered. This is done best by repeatedly dilating the anal outlet in the postoperative period. Premature closure by healing skin can generally be opened by firm pressure of the examining finger tip. Later fistulae are best cured by introducing a small curved blade into the upper opening and drawing it out rapidly along the course of the fistula. Persistent dilatation until healing is completed in the desired fashion must be undertaken in all cases.

ALTERATION OF THE MUCOCUTANEOUS JUNCTION

The most important landmark in the anal canal is the mucocutaneous line, and preservation of its normal relationship to the anal outlet is a vital part of any procedure carried out in this portion of the intestine. Constant seepage of mucus and fecal contents from the lower rectum occurs when an ectopian-like protusion of secreting mucosa presents into the lower anal canal, the consequence of the surgeon's failure to approximate the dentate margins in a circumferential manner. The reverse of this may also develop in which skin is brought up too high, resulting in imbrication and retraction. Irregularities of this nature lead to imperfect closure of the anal lumen notwithstanding normal

3. Elkins, R. F., *South.M.J.*, 46:182-184,1953.

sphincteric function.

Use sharp scalpel dissection here rather than excision with scissors, no mass ligation, no undue traction on the internal hemorrhoidal bed. When infection develops, the administration of antibiotics, repeated digital dilatations and the local application of cauterizing solutions will occasionally benefit the patient. The best way is to excise the involved portion of the wall, free up the retracted or everted tissue, and reestablish the continuity of the mucocutaneous line at the proper level.[4]

PRURITUS

We consider here the occasional patient whose pruritic state can be traced directly to the period following surgery for benign anorectal disease. Such a history offers every reason for encouragement to the physician accustomed to dealing with this disheartening problem. The specific cause for the postoperative complaint is almost always based on either 1) a mechanical defect at the anal outlet, 2) a low-grade infection persisting from the time of the operative procedure, 3) allergic phenomena initiated by the application or injection of antiseptic or anesthetic solutions, or 4) a combination of any of the foregoing.

A history of postoperative itching warrants a thorough examination of the area about the mucocutaneous line. Diagnosis is obscured by the inflammatory dermatitis produced by scratching and application of various ointments and creams. Local applications of all kinds must be stopped, and the perianal area kept dry. Application of a 0.5 per cent aluminum subacetate solution three times daily will usually maintain a clean, dry anal outlet and control the irritation. In the more refractory cases the application of a one or two percent hydrocortisone acetate will produce remarkable results.

ANAL ULCERATION

An area of erosion in the anal canal after operative trauma is the manifestation of a localized focus of infection, resistant to the usual pattern of healing and epithelization. Ulcerated areas are much more common in the posterior midline, in the Y shaped triangular space. Lateral or anterior ulceration is most commonly the result of a disruption of the mucocutaneous line, or the reaction to the presence of a foreign body, a focus of granulation and secondary erosion.

In almost every instance, postoperative anorectal infection and ulceration originate and progress in tissue that has not been allowed to drain amply. Sufficient skin must always be removed here to retard healing and to prevent blockage of the drainage channels before the mucosa has united while areas susceptible to infection remain. Repeated dilatation is added insurance that such will take place.[5]

FECAL IMPACTION

Although this is one of the most common and distressing complications of the postoperative period, it is often overlooked. Pressure and congestion result in increase in pain and spasm; the mixture of feces, blood and serum offers an ideal medium for the growth of bacteria. Digital examination is the only exact way of diagnosing this condition.

4. Turrell, R., *S. Clin. North America*, 32:677-686, 1952.

5. Pontius, G. V., *S. Clin. North America*, 23: 255-290,1943.

One may be misled, however, when anal pain and spasm make this simple maneuver difficult.

Thorough cleansing of the lower rectum by repeated enemas prior to surgery, and utilization of the stool softeners (dioctyl-sodium-sulfosuccinate), will obviate impaction. If an impaction develops, the local administration into the rectal ampulla of either warm mineral oil or a solution of wetting agents, will cause sufficient softening for easy passage in most every instance. The use of harsh or irritating enemas, sodium peroxide or manual removal is to be avoided. Liberal amounts of the opiates should be administered prior to any attempt at dislodging the impaction, and extreme caution used when the enema tip is introduced into the anal outlet.◀

Central Nervous System Arteriosclerosis in Aging Patients

Metrazol was given for a period ranging from one to ten years to 687 patients, each of whom was observed for an average of two and one-half years. Over 206 gave a history of "small strokes" or were known to have had them. Approximately 10 per cent of these patients had primary psychiatric disorders including nocturnal delirium, confusional states, or agitated behavior with dementia and delusions. Many were essentially disabled by insecurity, weakness, and varying degrees of withdrawal.

Good to excellent results were obtained in 574 patients (83.5%), 82 patients (12%) were classed as failures because of lack of evidence of significant improvement. An additional 31 (4.5%) were labeled failures because of their inability to tolerate medication, indifference to dosage schedules, or willingness to discontinue medication. The improvement in sleep pattern, social adaptability, subjective feeling of well-being, freedom from symptoms, and lessening of disability make this therapy appear to be a safe and useful adjunct to the treatment of the arteriosclerotic individual.

Kapernick, J. S., *Geriatrics*, 12:703-708,1957.

Radioactively Labeled Vitamin B_{12} in the Diagnosis of Pernicious Anemia

Examination of the stained blood smear, calculation of red cell indices, and the demonstration of achlorhydria will make or confirm the diagnosis in most cases. If still in doubt, bone marrow aspiration and study of the smear will give the answer. Finally, an injection of vitamin B_{12} and evaluation of the hematologic and symptomatic responses will afford the evidence needed to make a diagnosis in the untreated cases of pernicious anemia.

This test requires some technical facility. For the patient it is simple and safe. It does entail the collection of a 24 hour urine specimen. The test requires facilities for handling radioisotopes and very sensitive gamma ray counting equipment. Radioactive cobalt has such a long half life that contamination with it becomes a serious laboratory problem.

This test is not to replace the tried and true methods for the diagnosis of pernicious anemia. It is useful in cases in which a variety of factors obscure the usual manifestations of the disease.

Smythe, C. M., *J. South Carolina M.A.*, 53:329-332, 1957.

ORIGINAL ARTICLE

Use of Steroids in Dermatology

The value of steroid therapy depends on a thorough knowledge of when they should be used, for how long, and correct selection of compounds

ROY L. KILE, M.D., *Cincinnati, Ohio*

Steroid hormone therapy has probably had as much impact on dermatology as on any other medical specialty. At the outset it should be stated that steroids never cure anything, but merely ameliorate symptoms. In some instances they may even cause a "rebound phenomenon" that is as bad as or worse than the original eruption, however these drugs sometimes afford great relief to the itching and burning of extensive eruptions. In a few skin diseases they may be life-saving.

It is probable that the steroids have been far overused in dermatology. A dramatic impression is made on the patient by the immediate clearing of the eruption. However the systemic steroids should be used in dermatology only for a limited number of diseases that are either causing a great deal of discomfort, or that might have serious consequences. Topical application of steroids can be used for many conditions, often very effectively.

INDICATIONS

Systemic steroids are for control of extensive, uncomfortable eruptions that are temporary in nature, *e.g.*, drug eruptions and acute contact dermatitis. Some severe and extensive drug eruptions, such as those that occur 10 days to two weeks after the administration of penicillin, can be controlled by a combination of

antihistamines and systemic steroids. This applies to any type of serum sickness type of reaction, regardless of the antibiotic or vaccine.

Of the many such combinations, methyl-prednisolone* has been most effective with minimal side reactions. In extensive cases either *Corticotrophin-zinc* or *Acthar* gel is usually given by injection, combined with methyl-prednisolone by mouth. In addition, antihistamines are given and soothing topical preparations are used. Acute contact dermatitis such as that from poison ivy, may be very effectively controlled, provided adequate doses are given. There is a definite "rebound phenomenon" in some cases of this condition, however. During the past year several such eruptions persisted for several months when steroids were given early in the course of the disease, but discontinued too soon. In some instances they have been given rather irregularly. When they were stopped, the eruption recurred in all of its severity, at times worse than the original attack. Such eruptions may continue for several months, when ordinarily, with older methods of treatment, they would have responded in a few weeks. It has not been proven that this is entirely due to the steroids, but certainly one would suspect them. However, in the rather acute cases it is still the author's practice to employ such drugs, carrying them on for at least a week after the eruption has disappeared. Then they are very slowly withdrawn.

ERYTHEMA MULTIFORME

In extensive cases of erythema multiforme the steroids are most effective. The same combination of methyl-prednisolone and ACTH preparations by injection have been employed.

LUPUS ERYTHEMATOSUS AND PHEMPHIGUS

In acute cases of such diseases as lupus erythematosus disseminata and phemphigus, the drugs employed systemically are at times life-saving. Other preparations should be given simultaneously, so the individual may be taken off the steroids as soon as possible—the basic premise in any chronic disease. Many patients who have had the steroids over a period of one to two years have developed drastic personality and physical changes, including Cushing's syndrome. These are often difficult to control and slow to reverse. This is one of the principal reasons against the promiscuous use of steroids by so many in the practice of dermatology. As new compounds are developed that produce fewer reactions perhaps this situation will change for the better.

TOPICAL USE

While cortisone is effective systemically, it has no effect when applied to the skin surface. However it is effective when applied to the eye. Hydrocortisone is effective when applied to the skin's surface, and so used has proved of great value in dermatology. When employed in comparable strengths, none of the new steroid compounds has been found to be superior to hydrocortisone for topical application.

COMBINED WITH ANTIBIOTICS

In infections a combination with antibiotics has been most effective. Neomycin, Terramycin, Bacitracin, and many others have been employed

*Medrol, The Upjohn Company, Kalamazoo Mich.

in combination with hydrocortisone. Their indications are many and varied, and numerous inflammations of the skin will be helped by such applications. In psoriasis, the help is transient. Some fungus infections seem to be aggravated.

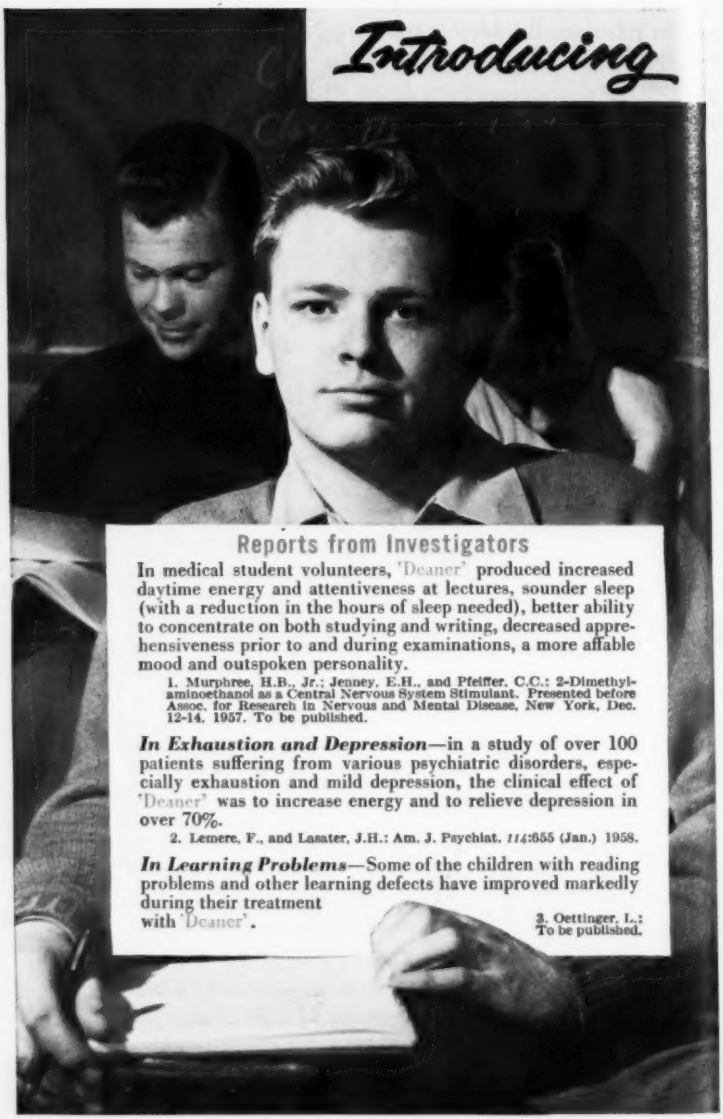
OTHER STEROID PREPARATIONS

Fluorohydrocortisone has some very definite indications for topical application in dermatology, though it is not used systemically, it may be a very effective drug. The only fear is that of absorption through the skin. This is a very real danger, much more apt to occur when lotions are applied over large areas. On small areas, and using the ointment, one need not fear this complication.

Prednisolone and delta-hydrocortisone have been found very effective for topical use. It is not believed that they are superior to hydrocortisone for this purpose.

Topical applications of methylprednisolone have been found to be as effective as any treatment used in this manner. For the first time, a preparation that may be superior to hydrocortisone has been found. This drug is employed in a 0.25 to 0.5 per cent strength in a vaseline base.* Combined with Neomycin† it is also very effective in controlling some topical inflammations as well as infections. In time, it is felt this preparation will be one of the most effective drugs available. Certainly many more such improved preparations are to follow and better therapeutic agents will be ours to use in the near future.◀

*_Medrol Ointment_, The Upjohn Company.
†_Neo-Medrol Ointment_, The Upjohn Company.



Reports from Investigators

In medical student volunteers, 'Deaner' produced increased daytime energy and attentiveness at lectures, sounder sleep (with a reduction in the hours of sleep needed), better ability to concentrate on both studying and writing, decreased apprehensiveness prior to and during examinations, a more affable mood and outspoken personality.

1. Murphree, H.B., Jr.; Jenney, E.H., and Pfeiffer, C.C.: 2-Dimethylaminoethanol as a Central Nervous System Stimulant. Presented before Assoc. for Research in Nervous and Mental Disease, New York, Dec. 12-14, 1957. To be published.

In Exhaustion and Depression—in a study of over 100 patients suffering from various psychiatric disorders, especially exhaustion and mild depression, the clinical effect of 'Deaner' was to increase energy and to relieve depression in over 70%.

2. Lemere, F., and Lasater, J.H.: Am. J. Psychiat. *114*:555 (Jan.) 1958.

In Learning Problems—Some of the children with reading problems and other learning defects have improved markedly during their treatment with 'Deaner'.

3. Oettinger, L.: To be published.

ORIGINAL ARTICLE

Operating Room Deaths

Institution of a definitive plan of action based on the utilization of procedures such as are presented here may reduce the mortality rate

KENNETH K. KEOWN, M.D.* and
HUGH E. STEPHENSON, JR., M.D.,* *Columbia, Missouri*

Preventable deaths occur all too commonly in the operating room. Most instances of cardiac arrest are preventable. Cardiac arrest, cardiac stand-still and cardiac asystole are synonyms. Operating room fatalities from cardiac arrest have been reported since 1846.[1] In 1898, attempts were made at manual heart compression to resuscitate a patient who suffered cardiac arrest during the administration of chloroform by means of the open drop technique.[2]

The Philadelphia Anesthesia Study Commission (a group of interested physicians studying all deaths that occurred during or within 24 hours after anesthesia) reported their findings in 1947.[3] The conclusions were that deaths could not be attributed to a single anesthetic agent or technique. Fatalities resulted most commonly from errors in the administration or management of the anesthesia and improper pre-anesthetic preparation and evaluation.

A Cardiac Arrest Registry[4] is maintained at the University of Missouri Medical Center to collect the pertinent data of each operating room fatality from every accredited hospital in the

*School of Medicine, University of Missouri.

1. Snow, J., *Chloroform and other Anaesthetics*, John and Churchill, London, 1858.
2. Tuffier & Hallion, *Bull. et Mém. Soc. Chirurgiens, Paris*, 24:937,1898.
3. Ruth, H. S., et al., *J.A.M.A.*, 135:881-884,1947.
4. Stephenson, H. E., Jr., et al., *Ann. Surg.*, 137: 731-744,1953.

United States. These data shed further light on the multiplicity of factors involved in cardiac arrest.

The tabulations from the Cardiac Arrest Registry, the Philadelphia Study Commission, the literature[5-6] and the authors' experience[7] clearly point to one or more of the following etiological factors existing immediately prior to cardiac arrest:

Anemia

The inability of the body to store oxygen points to the need of a hemoglobin determination of at least 10 gm. per 100 ml. of circulating blood prior to instituting anesthesia for any elective case.

Anesthetic Overdosage

All anesthetic agents and techniques have been implicated repeatedly as the cause of operating room fatalities. Most blame should be directed at overdosage. All anesthetic agents are myocardial depressants when administered in excess.

Anoxia

This may be from respiratory obstruction, existing pulmonary disease, or congenital or acquired cardiac lesions. The cardiac lesions most commonly causing cardiac asystole during anesthesia and surgical procedures are aortic stenosis, coronary artery disease, and myocardial disease. Anoxia is the single most common factor predisposing to cardiac arrest.

Inadequate Preliminary Medication

Adequate preliminary medication is essential to allay fear. Apprehensive patients exhibit a materially increased cardiac output with a concomitant increase in cardiac effort. This is produced by abnormally high blood concentrations of endogenous epinephrine and norepinephrine.

Intravenous Administration of Unlabeled Drugs

A careful check of the label of the container before administration of any drug is fundamental.

Every drug to be administered during the course of anesthesia in a surgical procedure should be doubly checked, to see that it is the desired pharmacologic agent, and that the proper dose is to be administered. Epinephrine is frequently confused with ephedrine, pituitrin with pitocin.

Metabolic Diseases

Several of these may have existed prior to the induction of anesthesia, prominent among them are unrecognized diabetes, Addison's disease and hypothyroidism.

Postural Changes

Sudden shifts of position of patients under anesthesia predispose to hypotension. The anesthetist may be so busy securing the previously anesthetized patient in the proper position for the operation, that cardiac arrest or hypotension may go unrecognized for periods of one to four minutes. The anesthetist should not be made responsible for securing the anesthetized patient. His attention should be directed solely to the maintenance of as nearly a normal physiological state as is possible.

Reflexes

Reflexes originating from anesthetic and surgical techniques include those resulting from endotracheal intubation, aspiration of the tracheal bronchial tree, traction on abdominal

5. Reid, L. C., et al., *Arch. Surg.*, 64:409-420,1952.
6. Ruth, H. S., et al., *J.A.M.A.*, 164:831-836,1957.
7. Stephenson, H. E., Jr., et al., *Arch. Surg.*, 69: 37-53,1954.

viscera, kinking or torsion of great vessels, or sudden release of increased pressures within the abdominal or thoracic cavity.

Unlabeled Gas Cylinders

The gas manufacturers are not responsible for the correct coloring of their gas cylinders. They are responsible for proper labelling of gas tanks. It is each anesthetist's responsibility to carefully read the label on each cylinder prior to utilizing the agents that are contained. This should be done prior to the induction, not during the course of anesthesia.

Two or more of the precipitating factors are usually present whenever operating room fatalities occur. It is unfortunate that errors are most usually compounded during the course of a trying anesthesia and operation.

Cardiac stand-still may occur at any time during the course of anesthesia. The most frequent periods for its occurrence are those of induction and emergence, unless shock or surgical complications are present during the maintenance. Cardiac asystole occurring late in the anesthetic phase or during emergence from anesthesia may be due to anemia, a decrease in the volume of circulating blood (from unrecognized surgical blood loss), late effects of anesthetic overdosage, carbon dioxide excess, reflexes initiated by extubation with a depletion of the oxygen intake by the aspirating catheter being placed within the tracheobronchial tree, and oxygen deprivation regardless of the cause.

SUGGESTIONS

There are several protective measures that are important. Since most "anesthetic deaths" may be avoided by constant surveillance of the anesthetized patient, the following suggestions are helpful and may be used as guides in the prevention or avoidance of this catastrophe.

ADEQUATE TRAINING IN ANESTHESTIC ADMINISTRATION

This is essential for the more complicated and difficult types of surgical procedures, such as radical surgery for carcinoma, intracardiac surgery, surgery in the geriatric patient and intracranial surgery.

PRE-ANESTHETIC PHYSICAL EXAMINATIONS

Pre-anesthetic physical examinations with pertinent laboratory information should be *recorded* prior to the induction of all anesthetics. The necessary laboratory determinations are urinalysis and hemoglobin estimations within 48 hours of onset of anesthesia. If a patient is brought to the operating room improperly prepared, it is the responsibility of the anesthetist to bring to the surgeon's attention the existing discrepancies. Last minute cancellation of surgery is far preferable to jeopardizing a patient's life. The cancellation of a case should be decided by mutual agreement between the anesthetist and the surgeon.

The anesthetized patient should be under constant surveillance, and the status known to the anesthetist at all times. It must be realized that asystole or arrest or cardiac stand-still can occur even while the anesthetic is being administered by the most skilled technicians.

All members of the operating room team should be well versed in a proper program, so that whenever cardiac asystole occurs, immediate action that is premeditated and previously practiced can be instituted.

Time is of the utmost importance. The body has no store of oxygen, therefore, institution of therapy after a delay that exceeds four minutes is usually futile.

WARNINGS AND RESPONSES

Hypotension or lack of adequate cardiac output is first noted by the anesthetist as lack of adequate carotid artery pulsation. Without a moment's delay the surgeon is informed of the patient's condition. The anesthetist must waste no time checking blood pressure equipment. The operating room is no place to keep secrets when a life is in the balance. The surgeon notified, the anesthetist discontinues the administration of all anesthetic and intravenous agents. The breathing bag is emptied of other gases, filled with oxygen and the patient's lungs thus inflated with oxygen. The anesthesia machine is utilized as a respirator. The respiratory rate is maintained at 20 per minute, and at least 500 ml. of oxygen inflated into the tracheobronchial tree with each manual compression of the breathing bag.

The surgeon bares the patient's left chest, and cuts through the skin. If bright red blood flows, the incision is carried no further. If not the incision is made into the chest, the left lung retracted, and inspection of the pericardial sac reveals whether the heart is at a stand-still, is contracting weakly, or is in a state of ventricular fibrillation. Regardless of the finding, the heart is compressed between the thumb and fingers, expelling a quantity of blood into the great vessels with each compression. If the heart has ceased to contract, or is about to cease, rhythmic compressions through the intact pericardium may restore effective cardiac action within a few seconds, as adequate respirations are maintained by manual compression of the breathing bag by the anesthetist. Within a short time, the heart should begin to contract simultaneously with the manual compression. There are but two drugs to restore cardiac action—epinephrine hydrochloride and oxygen. The former should be injected into the left atrium or left ventricle. Although oxygen is not truly a cardiac stimulant, a continuous supply is essential.

FIBRILLATION

Ventricular fibrillation is best controlled by electric counter-shock. Electric shock to the heart is not a means of restoring cardiac action *per se*. It is solely the means of controlling ventricular fibrillation, and the restoration of normal action is dependent upon prompt manual compression that is adequate to maintain a systemic systolic blood pressure of 80 millimeters of mercury or more.

Ordinary house current can be utilized to control ventricular fibrillation. The electrodes are placed one over the right, the other electrode over the left, ventricle, and the current shot through. It may be necessary to increase the voltage to 200 with a decrease in amperage. The amperage should never exceed six.

CONCLUSION

The presence of proper equipment should be assured prior to the induction of anesthesia. The essential items are a laryngoscope, endotracheal catheters, solutions of atropine sulphate, epinephrine hydrochloride, and lidocaine hydrochloride, with appropriate syringes and needles. It has been possible to save most all of the patients who have developed cardiac asystole by following the procedures that have been presented.◀

ORIGINAL ARTICLE

Use of A Combination of Progesterone, Testosterone, and Estrone in the Treatment of Pityriasis Rosea

Intramuscular injection of this combination relieved all 13 patients after the first injection, and they were free of symptoms in less than a week

MICHAEL GRATCH, M.D.,* *Maytown, Pennsylvania*

Pityriasis rosea (herpes tonsurans maculosus of Hebra) is an acute, self-limited, mildly inflammatory dermatosis, characterized by numerous papulous squamous lesions, usually preceded by an initial plaque one to two weeks before the outbreak of the rash. As a rule, there are no systemic symptoms, but malaise and fever of a low grade sometimes occur. Itching is a frequent symptom. The rash is usually localized to the trunk, the head and extremities being rarely affected.[1] Different investigators have reported the duration of this dermatosis as varying from 2½ to 8½ and even 14 weeks, with or without treatment.

Treatment commonly consists of mild ointments and lotions, ultraviolet light, hydrocortisone ointments and lotions—all with varying results. There is no systemic treatment.

A white woman, age 37, presented herself with a complaint of functional

*St. Joseph's and Lancaster General Hospital, Lancaster, Pa., Columbia Hospital, Columbia, Pa.

1. Percival, B., *Brit. J. Dermat.*, 44:231,1932.

amenorrhea. A papulo-squamous eruption resembling pityriasis rosea was observed on her trunk.

She received a series of three injections, consisting of 25 mg. progesterone, 25 mg. testosterone, and 6 mg. estrone in sterile saline solution,* because of her amenorrhea. She reported that the rash began to fade a few hours after the first injection but reappeared the following day, after which she received a second such injection. The following day the rash had completely disappeared, although another injection was given because of the concurrent condition.

It was decided to try a similar routine in future cases of pityriasis rosea and during a period of 18 weeks, 12 additional patients were treated in a similar manner.

One injection was given intramuscularly at two-day intervals. Invariably, after a period of a few hours to 48 hours, there was considerable fading of the rash. In most cases the rash disappeared after the second injection. No external or internal medications were given in any case. One man had a recurrence of one single eruption after the second injection, but this was cleared by a third injection.

CASE HISTORIES

Case 1

A construction worker, 32 years of age, had a dermatosis involving the trunk, resembling pityriasis rosea, for one week. A single eruption appeared on the neck a few days previously, with moderate itching and discomfort. The patient had never suffered from allergies or dermatoses of any kind. Two injections were given at two-day intervals. On the fourth day the rash had subsided. Two days later on the left arm a single eruption appeared, which disappeared after a third injection.

Case 2

A housewife presented herself because of a single plaque the size of a penny in the right scalenus anticlus region, which resembled an initial plaque of pityriasis rosea. Injections were given at two-day intervals. Four weeks after the second injection the patient showed no manifestations of pityriasis rosea.

Case 3

A woman, aged 22, in her 6th month of gestation, complained of a dermatosis involving trunk, abdominal wall and upper extremities with moderate itching, resembling pityriasis rosea.

Three injections were given at two-day intervals, although the rash had completely disappeared on the fifth day.

Case 4

An unmarried nurse, age 22, gave a history of a single, nummular, papulo-squamous eruption on the neck. One week later the rash had become generalized on the trunk and upper extremities.

A series of three injections was given. On the 4th day the rash had disappeared.

SUMMARY

This is a preliminary report on a series of 13 patients ranging from 20 to 40 years of age, suffering with pityriasis rosea, who were treated with a combination of 25 mg. progesterone, 25 mg. testosterone, and 6 mg. estrone in 1 cc. of sterile saline *(Tristerone)* given intramuscularly, in a series of from two to three injections at two-day intervals.

All the patients were relieved after the first injection and free of symptoms after the third—all in less than one week.

With symptomatic treatment or without treatment, the condition may last several weeks.

This report will be followed up with more clinical investigation. One point of interest is the suggestion of the possibility that pityriasis rosea may not be a separate entity, but rather a symptom or manifestation of endocrine imbalance or disturbance.◀

*Tristerone,® Wyeth Laboratories, Philadelphia.

ORIGINAL ARTICLE

Allergy To Bees and Wasps

Venom has an action similar to histamine; when a patient has become sensitized, immunization should be instituted for long-term protection

HALLA BROWN, M.D.,* *Washington, D.C.*

It has been known for thousands of years that large numbers of bee stings can kill a man. It has been recorded occasionally, since 2655 B.C., that a single sting of wasp or bee has killed an adult human.[1] This effect depends, not directly upon the quantity of toxin administered, but on the venom acting as an antigen, combining with antibody (reagin) which the patient, sensitized by a previous sting, has already formed.

Cases of allergy to insects or their products have been reported with increasing frequency since 1765 when the death of a person some minutes after a single sting above the eyebrow was reported.[2] In 1949 Swinny noted seven deaths reported by the Texas Bureau of Vital Statistics.[3] He estimated 20 to 30 deaths and 200 to 300 cases of non-fatal anaphylaxis yearly in Texas from insect allergy. Possibly some persons are stung fatally when alone and their deaths are attributed to "coronary occlusion" or "natural causes".

Cases of insect allergy must be differentiated from those, numerous in the European literature, of asphyxia, where a person has gulped down an insect with his wine, beer,

*Assistant Professor of Medicine at The George Washington University.

1. Waddell, L. A., Egyptian Civilization, London Luzac and Co., 1930.

2. Desbrest, Journal de Medecine, Chirpham, Paris, 1765.

3. Swinny, B., *Texas J. Med.*, 46:639,1950.

or cider, and been stung on the palate, tonsil, or posterior pharynx. Most of these deaths probably were caused by asphyxia from the swelling which in this location obstructed the airway.

Over 30 species of insects are known to have caused allergic symptoms—anaphylaxis, urticaria, asthma, peripheral neuritis, the Arthus phenomenon, and various eruptions.

MORBIDITY OR MORTALITY

Insects may cause morbidity in at least four different ways:

1. The local swelling caused by the toxin may block off the airway and asphyxiate the patient.

2. An insect may inject its toxin into a vein; *e.g.*, a bus driver was stung by a yellow-jacket in a vein on the back of the hand as he held the steering wheel.

3. Certain insects as the Mayfly and the Caddis fly, by shedding their wing scales in great numbers, cause inhalant asthma in sensitized patients. An occasional patient allergic to bee sting develops asthma in proximity to hives or to clothing worn by an apiarist.

4. An insect may inject its venom into a patient who has become allergic to it, *i.e.*, developed reaginic antibodies against it—the type which is the subject of this report.

In addition, it has been reported that pollen, introduced from the surface of an insect at the time of puncture, may cause symptoms in a patient allergic to that pollen.

SOME PARTICULARS

Among the bees only the workers need be feared. The drones can not sting, nor does the queen who, although capable of stinging, stings only a younger and menacing queen. The worker's entire stinging apparatus (stinger and sac) remains in and attached to the patient after the bee has flown off, soon to die. The smooth-muscle wall of the venom sac contracts spontaneously and pumps any remaining venom into the victim. Two to three minutes are required for the entire contents to be injected.

Members of the vespid family (wasps, hornets, yellow-jackets) have a smooth curved stinger. Wasps do not lose their stinger and, after withdrawing it, may encircle the victim to sting again a number of times.

For reasons unknown, some hives are gentle, and the insects sting only when an individual or the hive is threatened. Others are aggressive, stinging without apparent provocation. Yellow-jackets, notorious for their combativeness, will return to bombard the victim, and, if enclosed in a trouser leg, will sting repeatedly. Yellow-jackets bite as well as sting. The bite is used merely to get a better hold for stinging. The venom of wasps and bees is composed of a secretion from an acid gland combined with that from an alkaline gland. Various contradictory reports of its contents have been published, and the subject needs reevaluation. There is little doubt that venom has a histamine-like action.

A Typical Case Report

A boy of 16 was stung by a bee in 1952 without abnormal reaction. In 1953 he was stung by a bee or wasp on the foot with the development of an enormous swelling lasting three days. In the early fall of the same year he was stung again while picking apples off the ground, this time on the finger. Promptly his hand swelled, and in 15 minutes he broke out in hives. A short while later his breathing became difficult. Epinephrine almost immediately relieved

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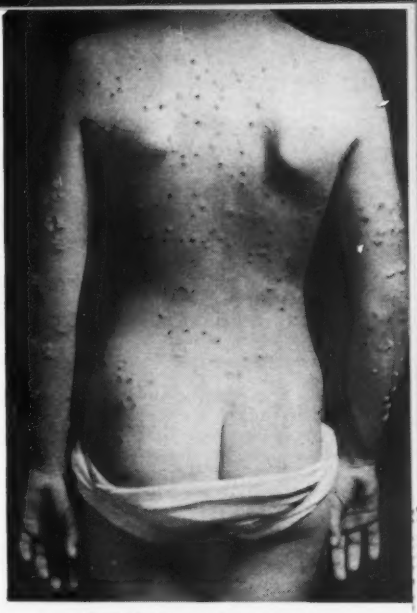
M., Local treatment of psoriasis, including a review of al literature, *M. Times*, 85:1397, (Dec.) 1957.
el, I. H., New local treatment for psoriasis, with report of es, *M. Rec.* 151:397,1940.

*T. M. Reg. U. S. Pat. Off.



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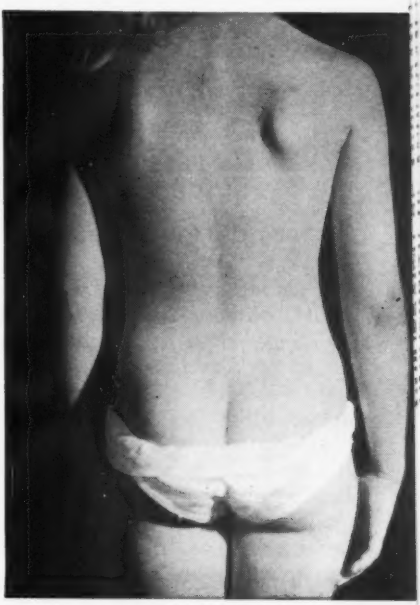

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IASOL FOR PSORIASIS

the symptoms. In 1954 he was stung on the back of the neck by a yellow-striped insect. Within five minutes he was covered with hives, felt weak, had difficulty in breathing, and lost consciousness. Injection of epinephrine again brought about relief, but more slowly and less completely, and the patient was hospitalized overnight.

The patient was seen for allergic diagnosis one month later. Examination revealed a normal boy, blood and urine examinations negative, skin tests to bee antigen negative, but those to yellow-jacket 1:10,000 four-plus. Tests to wasp, hornet, etc. were equivocal. The patient was immunized at weekly intervals until the maximum dose that he tolerated was reached. This was 0.4 cc of 1:10 extract of yellow-jacket antigen. Any increase in dose gave him a painfully sore arm for two days. This maintenance dose was repeated at a weekly, then biweekly, then triweekly interval. From then on the patient received the same dose every four weeks throughout the year.

In 1955 the patient was stung by a honey-bee without reaction. Later that summer he was stung by a yellow-jacket with a moderate local swelling lasting 24 hours. At the time he took an antihistaminic by mouth and placed a *Nephenaline* tablet under his tongue as a precautionary measure. In 1956 he was stung again by a yellow-jacket without local or general symptoms. On this occasion he took no medication. Blood count is still normal, and no untoward effects of immunization have been observed after three years.

TREATMENT OF INSECT-STING ALLERGY

When stung by a bee, the patient should, without delay, scratch out the stinger with its attached venom sac, in the direction opposite to that from which the stinger entered. To pick out the sac with thumb and forefinger, or with tweezers, is to squeeze more venom into the sting site. If stung by a hornet, wasp, yellow-jacket, or bumble-bee, the patient needs to get under cover quickly so he will not be stung again. Then an antihistaminic should be swallowed—if a liquid, the patient should have been told in advance how many gulps from the bottle make a 50-100 mg. dose of the older antihistaminies (tripleenamine, diphenhydramine, etc.), or an 8 mg. dose of *Chlortrimeton*. Immediately thereafter the patient should place a tablet of *Nephenalin* under his tongue, hold it there for 5 minutes (count slowly to 300) to absorb the Isuprel coating, then swallow it so that the ephedrine, theophyllin, and barbiturate may have a more lasting effect. If swallowed too soon, the patient will vomit from the irritating effect of the isopropylarterenol coating and thus lose the effect of the medication. The patient may prefer epinephrine (1:1000, 0.5 cc. subcutaneously) to *Nephenalin*, but for most patients, especially children, the use of *Nephenalin* is more practical. A few tablets can be kept at school, at home, in the glove box of the car, or in a locket about the patient's neck. Once these emergency measures have been taken, the patient should be taken to a doctor's office or to a hospital emergency room in case further care is necessary. If a finger or toe is stung, a tourniquet can be applied above the lesion to slow absorption. Stings on the head and neck are particularly dangerous.

PROPHYLAXIS

This includes avoidance and immunization. Once a patient has become sensitized, immunization should be instituted. While this is being accomplished, the patient should avoid exposure to stings.

Hives near the home should be removed. Before sitting down the patient should examine the ground for yellow-jacket nests. Since yellow-jackets are carnivorous, areas where there were picnickers should be avoided late in the day. Bathers in clover-surrounded pools should be

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well covered by terrycloth robes after emerging.

IMMUNIZATION

For long-term protection immunization is the best treatment. Beekeepers have used it in crude form for centuries. Upon finding themselves developing urticaria after a sting, they allow a bee to sting daily for progressively lengthening periods (seconds) until they are able to tolerate 3-minute stings without symptoms. This practice, although sound immunologically, is dangerous in a very sensitive patient.

There appears to be one antigen common to all wasps and bees but each species has in addition one (or more) distinctive antigens of its own. Most commercial extracts are made from the whole insect, since this procedure is easier than dissecting each venom sac. Some investigators, however, are convinced that the venom alone is the best antigen and that it should not be diluted with other body antigens. It has been stated that an extract containing bee and wasp antigens should be used in every case, because patients frequently identify the insect erroneously or call it by a local name.[4] Others believe that only an antigen to which the patient is proven sensitive should be used. If the insect cannot be identified with some certainty, it is probably safer to immunize with a mixture of bee and wasp antigens.

It is important that the insect be identified and a "treatment set" against that insect be purchased.* It is usually recommended that the patient be skin-tested with a dilution of 1:10 million or 1:1 million. If the test is positive, but gives less than a 4-plus reaction, treatment can be started with that dilution. Schedules enclosed in treatment packages may be followed safely in most cases. Special practices, such as the rapid, one-day intracutaneous immunization, should be left to specialists in the field.

What the top dose should be is not definitely known. Most commercial extracts contain 50% glycerine in the 1:10 dilution. Most patients cannot tolerate more than 0.3 cc. of this strength because of the irritant property of glycerine, even when diluted with saline in the syringe. When fresh venom (not commercially available at present) is used, the patient can be given an amount equal

MAINTAINING IMMUNIZATION

Once the maintenance dose has been attained, it is wise in some circumstances to sting the patient under controlled conditions in the office. If the patient is found to be protected, one has only to maintain immunization. The maintenance dose is repeated usually at 4-week intervals (in very sensitive cases at 3-week intervals) through the entire year, by some for 3 years routinely. Others consider the degree of protection the patient receives from immunization, the number of stings that received post-immunization and his reaction to them, the hazard of his occupational exposure, etc. We are safe in maintaining immunization for several years. The success of immunization cannot be stated in fig-

*Among suppliers of extracts are: C. E. Blatt, Independence, Mo.; Center Laboratories, 16 Sintsink Drive, East, Port Washington, N. Y.; Cutter Laboratories, 4th and Parker Sts., Berkeley 10, Calif.; Hollister Stier Laboratories, 2031 N. 63rd Street, Phila. 31; Sharp and Sharp, 3402 Norton Avenue, Everett, Wash.; SW Mold Laboratories, 1009 NE 17th Street, Oklahoma City, Okla.; Steman Laboratories, 1205 NE 18th Street, Oklahoma City, Okla.

4. Mueller, H. & Hill, L. W., *New England J. Med.*, 249:726,1953.

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ures.[5-7] However, there are numbers of case reports to attest unequivocally to its merit. We do not know the incidence of insect allergy, the duration of sensitivity, the causes of personality differences in hives (it is not the food eaten by the bees), their attraction to certain humans who again and again are singled out of a group to be stung, the best method of immunization (subcutaneous or intracutaneous) etc. Still less is known about bumble-bees. Nor do we know a repellent effective against wasps and bees.◀

5. McLane, E. A., *Minnesota Med.*, 26:1061,1943.
6. Fisher, D. C. & Center, C., *J. Allergy*, 5:519,1934.
7. Braum, L. I. B., *South African M. Rec.*, 23:408, 1925.

Intentional Replacement of Bacteria Following Antibiotic Therapy

A woman of 62 with a partially obstructing carcinoma of the sigmoid colon was given 250 mg. of neomycin at four-hour intervals, together with saline laxatives for 48 hours before surgical intervention. Postoperatively, she was given parenteral penicillin, dihydrostreptomycin and aureomycin in average doses for three days. Antibiotics and Wangensteen suction were then discontinued, and oral feedings resumed.

On the sixth postoperative day, she had low abdominal pain and passed several loose stools, on the seventh an explosive diarrhea, intense low pelvic pain, distention and shock. Smears and cultures of the stool were taken, aggressive treatment with oral and intravenous antibiotics was begun immediately. Gastric suction produced large amounts of parenteral fluids. On the eighth day, pulse and blood pressure could not be obtained, and there was continuous rectal seepage of blood-tinged fluid.

Venesection was required for the administration of 7,000 cc. of fluid and blood daily. Blood pressure was normal in 24 hours, but the diarrhea persisted. Large doses of parenteral antibiotic were given on the third day of diarrhea. The stool cultures were not yet revealing. The severe pelvic pain and moderate fever suggested pelvic abscess.

On the fifth day of liquid stools staphylococci were demonstrated on direct smear. On the sixth and seventh an enema of aqueous suspension of normal fecal material from another patient was given. Within six hours of the first inoculation, the stools appeared more normal in color and consistency. Despite a mild exacerbation of diarrhea on the sixteenth, and bilateral thrombophlebitis of the legs on the seventeenth postoperative day requiring anticoagulant treatment, the patient was in good condition on the twenty-fifth day after surgery.

Improvement was coincident with the bacterial reinoculation and had not been apparent before, even though an appropriate antibiotic agent had been administered in large doses for 48 hours previously.

It is possible that in the future we may be able to control the normal microbial flora of the entire human body, utilizing the many complex biologic and chemical interrelationships of the resident population to ward off or displace microorganisms which are pathogenic for the human host.

Kersten, H. H., *J. Iowa M. Soc.*, 48:240-243,1958.

ORIGINAL ARTICLE

Diagnosis and Treatment of Common Lesions of the Breast

Some suggestions for methods of diagnosis and treatment of benign and malignant breast lesions

HERBERT H. DAVIS, M.D., *Omaha, Nebraska*

An understanding of breast lesions is important to the physician because of their frequency and because one of the common lesions is carcinoma. Women with breast disturbances see their physician because of pain or mild discomfort, a lump, a discharge from the nipple, or a recent deformity of the breast.

PAIN NO DANGER SIGNAL

Pain or tenderness in the breast is distressing to the woman but is not a danger signal. It is most common with chronic mastitis, fairly frequent in cystic disease, and infrequent in lesions of graver importance.

OCCURRENCE OF LUMP

A lump should be palpated with the flat of the hand. Every breast is lumpy. This is most noticeable in chronic mastitis. If, when compressed with the flat of the hand, a lump remains prominent, it is called a dominant lump. A dominant lump is characteristic of carcinoma, adenofibroma, and often of cystic disease. In an early stage, the only sure way to differentiate is by biopsy. Every solitary dominant lump of the breast in any age group from puberty on must be considered to be carcinoma until proved otherwise by immediate biopsy.

DISCHARGE

A thick brown, green, gray or white discharge indicates stagnation in dilated ducts. A discharge of milk may occasionally persist for a couple of years after birth of a child. A colorless serous or bloody discharge is of more serious import and indicates epithelial hyperplasia. It may be a single intraductal papilloma, a papillary carcinoma, or the papillomatosis of cystic disease.

DEFORMITY

A scirrhous carcinoma causes a drawing in the tissue about it, or of the nipple. A rapidly growing carcinoma or other tumor or cyst may protrude.

LESIONS

A fungating ulcer is usually carcinoma. In over 90 per cent of the cases, the lesion is chronic mastitis, cystic disease, adenofibroma, intraductal papilloma, or carcinoma.

PREMENSTRUAL CHANGES

Preceding each menstrual period there are changes in the breasts similar to but of much less extent than in pregnancy. There is swelling, heaviness, and often some discomfort due to hyperemia, edema and some acini hyperplasia. If this is marked it causes diffuse nodularity and tenderness. It may be localized or diffuse, in one or both breasts. It is commonly called chronic mastitis, which is a poor term as it is not an inflammation.

CYSTIC DISEASE

Cystic disease is extremely frequent in the premenopausal age. A lump or lumps, with or without pain, and occasionally a little discharge from the nipple occur. There may be one or several palpable cysts up to several centimeters in diameter. These are encapsulated, not tender or slightly so, fairly movable, and have resiliency. Microscopically there are varying degrees of epithelial changes in the ducts and acini. The epithelium may be flat or there may be hyperplasia and papillomatosis.

ADENOFIBROMA

Adenofibroma forms a solid dominant lump which is resilient, circumscribed, and very freely movable. It is usually a solitary lump but there may be several.

PAPILLOMA

Papilloma in a duct may cause a bloody or occasionally serous discharge from the nipple. It is usually in the central part of the breast. It may be palpable or there may be just an area to which pressure causes the discharge from the nipple.

BREAST CANCER

Carcinoma of the breast is a common, relatively radioresistant, malignant tumor which tends to spread early and widely. Each year over 20,000 women die of it in the United States. There is no way to discover it until it has grown to be a lump large enough to palpate. Unfortunately it is usually painless, which fact delays its discovery. The lump is infiltrating and so may not be moved about as well as a cyst or adenofibroma. If it is the common scirrhous type, it is hard and causes some drawing in of the tissues about it. Later there may be some retraction of the skin over it or of the nipple. Cells may get into the lymphatics and go to axillary nodes where they may be palpated, or to the internal mammary nodes, or get into the blood and spread to such distant areas as lungs, liver or brain.

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AGE MAY SUGGEST DIAGNOSIS

Age of the patient, statistically, gives an idea of the diagnosis but does not prove it in the individual case. Chronic mastitis occurs during the menstrual life of the woman. Adenofibroma is a lesion of young women, mainly 20 to 35 years of age. Cystic disease is very common from 35 to 50 years. Carcinoma is a disease of middle and old age. Between 40 and 50 years, two-thirds of the dominant lumps are cystic disease, one-third are carcinoma. After the age of 55 a dominant lump is nearly always carcinoma. Even at 20 to 30 years of age carcinoma may occur, so a biopsy should be taken of any dominant lump. It should be an excisional biopsy with immediate frozen section.

TREATMENT OF BENIGN LESIONS

Treatment of the distress and nodularity of chronic mastitis is unsatisfactory. No biopsy is necessary. Opinions vary greatly as to endocrine therapy, both as to whether or not to use it, and as to what to use. As nervousness is often a great factor, reassurance is usually effective.

If the lesion proves to be an adenofibroma the excisional biopsy is all that is necessary.

Biopsy is often all that is necessary in cystic disease. However I have had 18 per cent recur and need reoperation. In some, a segmental resection or simple mastectomy may be indicated.

Papilloma may be treated by local excision. Papillary carcinoma is treated the same as other carcinoma.

TREATMENT OF MALIGNANT TUMORS

The principle in the surgery of carcinoma of the breast is complete excision *en bloc* of all carcinoma before it has spread beyond the field of operation. If this is accomplished, the patient is permanently cured. Radical mastectomy is the usual treatment. It is very successful in removing the breast tumor and axillary metastases. About one-third of seemingly operable patients have metastases to the internal mammary nodes. These may be radiated. A few surgeons excise them in a so-called supra-radical mastectomy. Radiation therapy may greatly slow the cancer growth. Metastases to distant parts may be palliated by giving testosterone, or estrogen in the cases of elderly women, or even cortisone. Ablation of ovaries and adrenals, or of hypophysis may help about half of the cases.◀

Brain and Spinal-Cord Tumors In General Practice

Prompt diagnosis and neurosurgical intervention, if indicated, will improve mortality and morbidity statistics

FRANCIS A. ECHLIN, M.D., *New York, New York*

Over 50 per cent of brain and spinal-cord tumors are curable if they are diagnosed early.

EARLY SYMPTOMS AND SIGNS

Bearing the possibility in mind, a careful history and physical examination are the first requisites. Headache should not be dismissed lightly. Signs and symptoms of different tumors are extremely varied, since they depend largely on the nature and location of the growth. Preoperatively it may be impossible to differentiate a benign from a hopelessly malignant tumor. On the other hand, many tumors produce typical signs and symptoms months or even years before causing severe brain or cord damage.

The characteristic early manifestations of certain types of neoplasm should be kept in mind. For instance, there are the benign meningiomas which comprise about 13 per cent of brain tumors. Olfactory groove benign meningiomas cause loss of smell on one or both sides, often for years before the frontal lobes or optic nerves are pressed upon. Sphenoid-ridge meningiomas reveal themselves by a gradual prominence of one eye and a thickening of the bones of one orbit. The parasagittal meningiomas may produce a slowly increasing bony

hyperostosis of the skull. Suprasellar meningiomas cause a gradual loss of temporal vision in both sides. Meningioma almost anywhere in the brain may cause epileptic seizures for years before any other manifestations occur. Any of these symptoms should immediately make the doctor think of a meningioma.

This same type of tumor is also common in the spinal canal and causes a slowly progressive motor and sensory paralysis of the legs, or of all four extremities.

GLIOMAS

Gliomas constitute 40 per cent of all brain tumors. These tumors infiltrate the brain tissue. One variety, the astrocytoma, is slow-growing and may be cured if it is operated on before vital structures are involved. Two other varieties, the glioblastoma multiforme and the medullo-blastoma, are probably never curable regardless of how early they are found and treated. Usually one cannot distinguish between a curable and a non-curable glioma before operation, so in all cases early operation is urgently necessary. When the tumor involves the cerebral hemispheres, symptoms and signs will depend on the location and the increase in intracranial pressure.

PAPILLEDEMA

The most important early sign of increased intracranial pressure is swelling of the optic discs. Symptoms and signs due to local action of the tumor or sensory paralysis of the opposite side of the body are loss of sight in the opposite field of vision, loss of speech if the tumor is in the left temporal lobe of a right-handed person, personality change, and frequently, an epileptic seizure. General effects include headache and, as a late symptom, progressive drowsiness.

Gliomas of the cerebellum, particularly common in children, cause headaches, vomiting, and staggering gait. Papilledema occurs early. Over 50 per cent of these cerebellar gliomas are benign astrocytomas.

ADENOMAS OF THE PITUITARY

Very important are the pituitary adenomas, comprising 15 per cent of all brain tumors. One variety causes gigantism before puberty and acromegaly in later life. Pituitary adenomas produce a uniform ballooning of the sella turcica, temporal headaches, and later bilateral loss of temporal vision. Finally, they cause blindness and disturbances in water metabolism from pressure on the hypothalamus.

EIGHTH-NERVE TUMORS

The so-called 8th-nerve tumor deserves special mention, since it is easy to recognize and can be cured if diagnosed early. It causes deafness in one ear followed by numbness and weakness of the face on the same side. A staggering gait and papilledema occurs later.

There are also blood-vessel and other congenital tumors, many of which can be cured.

TUMORS OF THE SPINAL CORD

Spinal-cord tumors frequently cause sciatic pain and may be diagnosed as herniated disc. As they slowly enlarge they produce progressive loss of sensation and motor power below the level of the tumor. Over 50 per cent of spinal-cord tumors are benign meningiomas, or nerve-sheath tumors, which can be totally removed. Diagnosis must be made before motor and sensory paralysis becomes severe.

DIAGNOSTIC PROCEDURE

If a patient has symptoms or signs

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that suggest a brain tumor, never delay long before seeking the help of a neurologist or neurosurgeon. Diagnostic aids available are:

1. X-rays of the skull. These may be normal even with brain tumor, or they may show evidence of increased intracranial pressure, local changes in the bone by the tumor itself, enlargement of the sella turcica, displacement of the pineal body, or intracranial calcification. Any such changes call for complete neurosurgical investigation. X-rays of the chest should always be taken in brain tumor suspects to rule out a metastatic brain lesion.

2. An electroencephalogram should be made early. In most cases this will diagnose the presence and location of a glioma. However, it may fail to indicate a slowly-growing tumor such as a meningioma.

3. A visual-field and fundoscopic examination is always indicated.

4. If a brain tumor cannot be ruled out, or if this is a likely diagnosis, get the help of a neurologist or neurosurgeon without delay. Subsequent investigation will then depend on his decision, and may include an air encephalogram or ventriculogram which almost always gives an absolute diagnosis of the presence or absence of brain tumor, but rarely indicates what kind of tumor it is.

5. Arteriography, outlining the vessels of the brain with a radiopaque substance, is another valuable method of diagnosing brain tumors. It should always be used if one suspects a blood-vessel tumor.

6. Recently the radioactive isotopes have been employed in the diagnosis and localization of brain neoplasms.

FINAL DIAGNOSIS

Finally, the diagnosis of spinal-cord tumors calls for the early help of the neurologist or neurosurgeon. X-rays of the spine generally give little assistance, but should always be taken. A myelogram with pantopaque injected into the spinal canal followed by fluoroscopy and x-rays will almost invariably diagnose the presence and level of the tumor. By the time a spinal-cord tumor has caused symptoms it will give rise to a spinal block or filling defect in the myelogram.

Over 50 per cent of brain and spinal-cord tumors can be cured by early surgical treatment. However, cure depends on early diagnosis. Delay means more blindness, more paralysis, and more mental impairment, even though surgery may cure the patient. The malignant gliomas are incurable, but surgery plus x-ray therapy may prolong the patient's life from one to three years.◀

New York J. Med., 58:904-906,1958.

Blood Transfusion in Anemias of Chronic Diseases

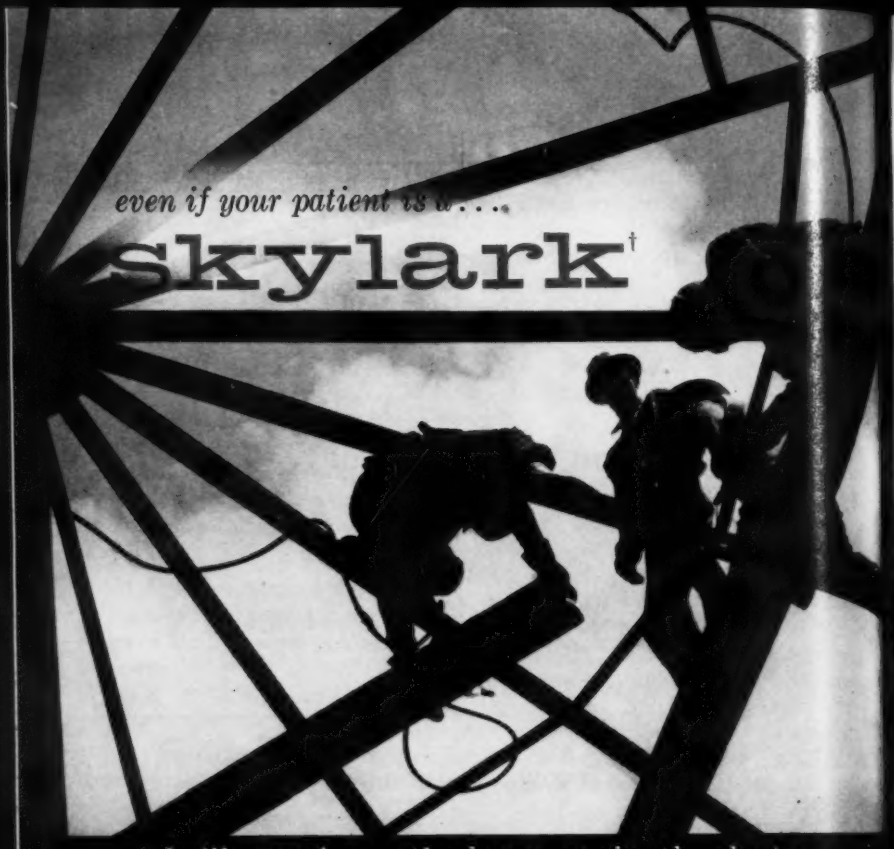
Blood transfusion is a valuable form of therapy and should always be used selectively rather than as a tonic or convenience

JACK J. RHEINGOLD, M.D., *Washington, D.C.*

Blood transfusion is one of the modern miracles of medicine. Much has been learned about blood groups, types, and sensitization, and cross-matching procedures have been improved. Rubber tubing and other reusable equipment has been replaced by disposable glass bottles, by silicone coated bottles, plastic tubing and plastic bags. All this has resulted in a tremendous increase in the use of blood transfusions. There is another side to the story which must also be considered—the fact that blood is over-used, despite the serious inherent dangers, in situations where the indications are vague. Indications for transfusion are:

1. Anemia produced by hemorrhage which is likely to recur.
2. Hemolytic anemia.
3. Aplastic anemia (also refractory anemia and leukemia).
4. Anemia of sepsis.
5. Any severe anemia in a surgical patient.

Bleeding from the bowel is a serious symptom and warrants careful investigation. Once the cause is known, the indication or lack of it for transfusion will be evident. The bleeding may be due to excision of a rectal polyp. The treatment of this iron deficiency anemia due to the blood loss is iron by mouth, not by



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transfusion. If the patient has ulcerative colitis or some other lesion where bleeding is apt to recur and the anemia continues or becomes more acute, the hematocrit should be raised to a safe level by transfusion. Bleeding from malignancies, colitis, diverticulitis and hemorrhoids, etc., must be considered separately when it occurs. Most patients with hemorrhoidal bleeding do not have severe anemias, and once there has been surgical correction, iron by mouth is the treatment of choice. A third indication for transfusion is the patient with a severe anemia about to undergo surgery. Blood plays an important role here in the treatment not only for the anemia, but occasionally in the treatment of shock as well.

Homologous serum hepatitis occurring several months after transfusion is a distressing complication. At the present time there is no routine, dependable method for screening out potential carriers except by careful history. As a result, this transmissible disease occurs regularly. Although it is said to occur in 0.45 to 1.0 per cent of cases, this figure may actually be higher because of unreported cases. Not only may chronic liver disease develop as a result, but the mortality from this disorder alone varies from 0.2 per cent to as high as 10 per cent in selected series. If the administration of incompatible blood is stopped as soon as symptoms develop, no serious harm may result. However, often renal failure develops along with hemolysis, hemoglobinuria and death.

A low hematocrit does not constitute an indication for transfusion when more conservative therapy is available. Blood must not be used as a tonic or as a convenience, nor should it be given for the "maintenance of the morale of anxious relatives."◀

Am. J. Proctol., 9:115-120,1958.

The Toxemias of Pregnancy

Prompt diagnosis of pre-eclampsia or eclampsia, together with adequate treatment, may carry the patient through to term

JOSEPH C. PARKER, M.D., *Richmond, Virginia*

There is confusion concerning the pathologic processes involved in the toxemias of pregnancy. The various changes described in the kidneys, liver and other organs are considered by some authorities to be the causes of the syndromes—others consider them to be the effects of the toxemic process.

Severe pre-eclampsia and eclampsia have one factor in common—aberration of the arterial vascular system. This is usually in its terminal branches, often vasospasm, mainly in the precapillary arterioles. This vasospasm may account for all of the changes observed in liver, kidneys, brain, heart, adrenals and other organs, as well as the symptoms and the biochemical alterations. The cause of this generalized vasospasm is not known.

DIAGNOSIS NOT DIFFICULT

The diagnosis of the toxemias of pregnancy usually is very simple. Pre-eclampsia when first noted is made manifest by a rapid, significant gain in weight in a woman past the 24th week of pregnancy with edema in hands and face, which is usually apparent on arising. Weight gain may be the only symptom when toxemia impends. Weight throughout pregnancy should be carefully watched, particularly after the 16th to 18th week.

If untreated, this rapid gain in

weight is followed by proteinuria and elevation in systolic and diastolic blood pressure, persistent, severe headache, visual disturbances, and swelling of hands, face, feet and ankles. In many instances urine output will be diminished. A large number of patients date the onset of their symptoms from some type of infection.

PRE-ECLAMPSIA AND ECLAMPSIA

Eclampsia is pre-eclampsia of severe nature, with added convulsions, coma, or both. A common indication of impending eclampsia in a patient with severe pre-eclampsia is development of a feeling of a girdle around the epigastric region. The patient is often a woman of extreme irritability, hypersensitivity to stimuli, who has twitching of various muscle groups. Usually blood pressure, proteinuria and edema are more severe preceding and accompanying the onset of convulsions and coma. In a large percentage of cases the appearance of eclampsia is complicated by oliguria or anuria.

DIFFERENTIAL DIAGNOSIS

Diabetic coma and insulin shock usually can be ruled out by history, blood sugar and urine sugar. Intracranial lesions, hemorrhagic or neoplastic, must be considered when there is any doubt of diagnosis. The question usually can be clarified by neurological examination, study of the eye-grounds, spinal fluid studies, and EEG. Epilepsy also can be ruled in or out on history and EEG findings. Usually the diagnosis of eclampsia is made on convulsions and coma occurring in a patient with preceding pre-eclampsia.

MANAGEMENT

Emptying the uterus is the best treatment in cases of antepartum or intrapartum eclampsia. Prophylaxis is adequate prenatal care, which embraces understanding and respect between the patient and her doctor, accurate determination of the patient's physical and mental state, as well as detailed study of the reproductive system, including pelvimetry and x-ray on specific indication.

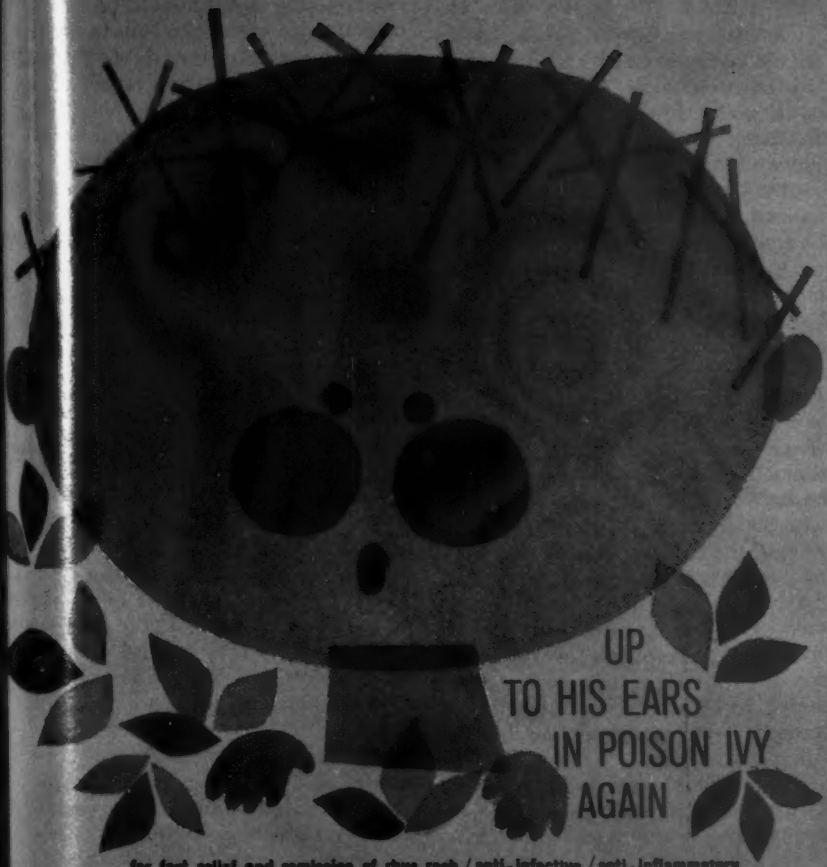
DIET

A dietary regimen must be outlined for all pregnant patients, and changed with varying conditions. After the 16th to 18th week salt limitation should be imposed with absolute proscription in the event of too rapid weight gain. Protein is included in adequate amounts, starches, fats and sweets are kept at a minimum. Pork should be taken in small amounts only.

REST ESSENTIAL

All pregnant women should have 8 to 10 hours of sleep at night and an hour or two of rest during the day —more for those tending toward excessive weight gain, nervousness, or vasomotor instability.

The patient should be seen every three weeks until the sixth month, every two weeks until the last month, and thereafter at weekly intervals. At prenatal visits the weight and blood pressure should be recorded and vaginal bleeding, fetal movement, edema, headache, scotomata, or any other unusual symptoms investigated. At frequent intervals the height of the fundus, the position and rate of the fetal heart should be ascertained, and signs of edema observed. The optic fundi require examinations at some time in the first trimester to have a basis for comparison later.



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1. Lubowe, I. I.: Am. Pract. & Digest Treat. 7:992, 1956.

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LABORATORY WORK

On the initial visit, hemoglobin should be determined, and r.b.c. done if it is low or high. W.b.c. and differential, complete urinalysis, blood type, Rh factor, and serological test for syphilis should be done. On each of the return visits, the urine should be examined for protein, with other studies on indication. The hemoglobin should be ascertained at 3-month intervals, more often if required.

All patients should have iron, calcium and vitamins as dietary supplements. If the blood pressure exceeds 140/90, or if the systolic rise is 25-30 or the diastolic rise 10-15, or if gain in weight is rapid or excessive or actual edema develops, the patient should be hospitalized immediately. For private patients who gain excessively in weight, the diet is 1500-1800 calories, with restriction of salt, increase of fluids, and some nonirritating diuretic such as *Diamox,* and magnesium sulfate, two teaspoonfuls every morning. Additional rest is ordered. If there is no improvement in two or three days the patient is hospitalized. All patients are instructed to report immediately any increase in severity of symptoms or the appearance of any new symptoms.

TREATMENT OF PRE-ECLAMPSIA OR ECLAMPSIA

Once pre-eclampsia or eclampsia has become established, the basic aims of treatment are to provide sedation and thereby allay convulsions, to promote vasodilation and combat vasospasm, to promote diuresis and to correct hemoconcentration. In these severe cases, the toxemic process must be brought under control before any type of delivery, either vaginal or abdominal, is contemplated.

A patient hospitalized in severe pre-eclampsia or eclampsia is taken immediately to the eclampsia room where a special nurse is on duty at all times. Blood is drawn for blood chemistry and electrolyte determinations. A Foley catheter is introduced and an accurate measurement of water intake and output is recorded. Through the same needle employed for the blood studies, 400 cc. of 10 per cent dextrose in water with 1.2 mg. digitoxin and one or two ampules of molar sodium lactate (depending on the level of the CO_2 combining power) are started slowly. Sedation with alternating doses of sodium pentobarbital and *Dilaudid* are given about every four hours. Careful attention is paid to respiratory rate with the use of sedation.

DELIVERY

This regimen is continued for 48 to 72 hours, if the patient is improving or remains static. At the end of this period the best method of delivery is determined. Many patients have *Pitocin* induction. Some are delivered vaginally, labor is induced by artificial rupture of the membranes if the cervix is negotiable and there is no obstetrical contraindication to vaginal delivery. Cesarean section is rarely necessary in a controlled eclamptic or severe pre-eclamptic patient. Many go into labor while under treatment.

TIME LIMIT

A patient with a severe toxemia who has not responded to treatment in 24 to 48 hours probably is not going to respond. Unless vaginal delivery seems feasible, the abdominal route under local, epidural or spinal anesthesia is usually employed.

CONCLUSION

The milder pre-eclampsias are

treated with less potent forms of sedation, on the basic principles outlined. Should a patient have recurrence of the toxemic process, it is again brought under control and the pregnancy terminated by the most expeditious means.

Some mild or moderately severe pre-eclamptics exhibit signs and symptoms of toxemia for long periods. The duration of hypertension has more prognostic significance than its severity. It is in the former type of case that *Pitocin* induction plays so helpful a role. In some of these cases induction fails after several attempts, and the cervix is not negotiable and abdominal delivery must be carried out.◀

West Virginia M.J., 54:83-87,1958.

Sternocleidomastoid Tumor of Infancy

Twenty-three of 1,283 consecutive newborn infants were found to have sternocleidomastoid tumors at two to seven weeks of age, an incidence of 1:56. The course in 11 was followed for from two to four years, and in nine for less than two years. None of these infants was operated upon and none has permanent deformity.

Line, F. G., & Line, M. L., *J. Tennessee M.A.*, 51: 133-135,1958.

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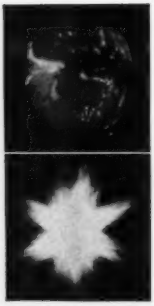

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References: 1. Weiner, H. H.: Clin. Med. *5*:25 (Jan.) 1958. 2. Decker, A.: New York J. Med. *57*:2237 (July 1) 1957. 3. Davis, C. H.: West. J. Surg. *63*:53 (Feb.) 1955.

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FINANCE

The Doctor Builds His Estate

Prepared for the readers of Clinical Medicine by the Research Department of the leading investment banking and brokerage firm of Bache & Co., 36 Wall Street, New York 5, New York

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These monthly articles point out one method by which the professional man may overcome the particular handicap imposed upon him by our tax structure, which taxes the bulk of his income at normal income tax rates, as opposed to the capital gains tax avenue open to many businessmen. One solution to this problem is the systematic investment of a portion of current income each year in securities. Such a program, which should include many different types of investments such as bonds, preferred stock, common shares and shares of mutual funds, will have as its objectives growth of principal together with reasonable income. We again emphasize that even the most complete series of articles of this type cannot take the place of consultation with a representative of a reputable brokerage firm.

There are two large groups of bank stocks in which institutional and other large private investors concentrate their holdings. One of these groups consists of the large "wholesale" New York City banks which are the principal depositories for the nation's large corporations. These banks, in turn, make a great proportion of the large loans to business. Interest-bearing savings or time deposits play a small part in their operations. The other major group of banks is made up of large "retail" California banks. This type of bank has many branch offices, and has a much greater percentage of interest-bearing time deposits.

In late 1956, the Federal Reserve

Board set the stage for what turned out to be a downturn in net operating earnings of banks with a great percentage of time or savings deposits. As of January 1, 1957, the Federal Reserve Board increased the maximum rate of interest that member banks might pay on savings or time deposits from 2% to 3%. Banks at that time were scrambling for funds, and short-term interest rates were climbing rapidly. For example, 91-day Treasury bills, perhaps the most widely-used indicator of short-term money rates, were then yielding more than 3%, compared to their present return of under 1%. Accordingly, many West Coast retail banks, led by Bank of America, quickly put the new 3% rate into effect on savings deposits.

The banks in making this move were confident that the newly attracted funds could be put to work profitably—that there would be sufficient demand from business for loans at rates well above 3% to enable the bank to make a profit on these new deposits. As 1957 wore on, interest rates topped out and began to decline. The high payments on deposits proved a drag on the earnings for many banks, and most California banks ended 1957 with unchanged or lower earnings than in 1956. The New York City banks, in contrast, scored impressive gains of 10% or more.

The cause of these divergent trends is obvious. In California banks, interest paid to depositors constitutes one of the largest expense items. Such interest came to 29% of American Trust Company of San Francisco's gross income in 1957 and to 28% of Bank of America's gross income, compared to only 3.7% for the Guaranty Trust Company of New York. These examples make the case clearly.

Of perhaps even greater significance to earnings was the fact that these payouts spurted sharply for California banks in 1957 due to the larger proportion of interest-bearing time deposits held by them. Thus, American Trust's interest payments rose from 20% of gross income to 29%, a rise of 9 percentage points, but an increase in actual dollar expenses for this item of almost 60%. Bank of America's interest payments on time deposits rose from 20% to 28% of gross income, an increase of 57% in actual dollar payments.

True, Guaranty Trust interest payments rose almost 32% in actual dollars, but this rise was from only a scant 3.2% of gross earnings to only 3.7%. What's more, a good part of this increase was due to interest paid on time deposits made by foreign banks, rates for which have already been cut this year, and interest paid on borrowings by the company to cover temporary deficiencies in the reserve required to be carried with the Federal Reserve Bank, deficiencies which have largely been eliminated by lower demand for funds and a reduced reserve requirement this year.

Since other expense items in 1957 remained relatively stable, the increase in interest paid on deposits reduced net operating profit margins of California banks by 10% or more in some cases while the margins of New York banks held roughly steady. For example, the net operating profit margin for Bankers Trust Company in New York actually rose from 21.8% in 1956 to 22% in 1957. A similar increase was scored by Chemical Corn Exchange Bank and First

National City Bank, while slight declines, generally less than one-half of 1% were noted in the operating profit margins of such New York institutions as Manufacturers Trust Company and Guaranty Trust Company. In contrast, net operating profits for California banks slipped noticeably, with Bank of America's net operating profit margin dipping from 20.1% to 17.4% and that of Crocker-Anglo National Bank slipping from 18.7% to 14.7%.

The low percentage of time deposits and below-average, steady operating expense ratios enabled New York City Banks to translate higher gross earnings into higher net income in 1957. These same factors, moreover, may well enable New York City banks to better withstand future reductions in gross income. Guaranty Trust Company's 23% pre-tax operating expense ratio and the Bank of America's 65% pre-tax operating expense ratio clearly point out the different leverage effect involved in these two issues.

Investors made eminently logical evaluations of these developments in 1957. Shares of major New York City banks worked higher during the year, and have continued to do so into 1958. California bank shares, in contrast, gave ground gradually during 1957, with a decline of between 17% and 32% from the 1956 highs recorded by year-end 1957. California bank stocks have recovered somewhat since the end of 1957.

Much of this strength in New York City banks probably stemmed from buying by investment groups. One compilation made of changes in common stock holdings of 53 investment groups shows that purchases of major New York City bank stocks in 1957 were both steady and sizable. At the same time, California and other western banks were almost completely avoided. By the end of 1957, bank stock holdings of the majority of reporting investment groups were heavily weighted in favor of New York institutions, while the large California banks had little representation as the result of a lack of new commitments and scattered selling during the year.

Despite all this evidence—in a sense, because of it—we believe a strikingly attractive investment opportunity is coming into existence. For one thing, the strength of New York City bank stocks is carrying them well into their near-term investment value ranges. In addition, we believe that a significant improvement in earnings lies three to nine months ahead for the California banks.

The cause of the expected improvement in California bank earnings obviously requires further explanation. On the face of it, with loan demand from business now tapering off, and interest rates, especially on short-term Government securities, softening, the high pre-tax operating expense ratios of California banks would contract new operating earnings even further, *unless the banks are able to cut expenses.* Here obviously lies the heart of the matter, for even a cursory glance at the profit and loss account of a large California bank focuses the eye immediately on one large item that readily lends itself to contraction—interest paid on deposits.

Naturally, competitive conditions from other savings institutions must be taken into account before a reduction in interest paid can be effected.

The most effective competition in the overall savings field comes from mutual savings banks, which are largely Eastern institutions concentrated in Massachusetts, Connecticut, Pennsylvania and New York. In California, in contrast, the savings and loan institution is the major competitor for savings.

Competition for savings in the West, however, is thus not only a competition of interest rates paid, but a competition of liquidity and convenience as well. Commercial banks and mutual savings banks both insure deposits under the Federal Deposit Insurance Corporation, while savings and loan institutions insure deposits under the Federal Savings Loan Insurance Corporation; there are certain differences in liquidity under the two insurance plans which favor the institution insured by the F.D.I.C. Since differences in liquidity and convenience compensate in some degree for the higher interest rates paid by savings and loan associations, the leadership in setting rates naturally is in the hands of the group with the largest proportion of savings in a given area. Whereas in the New York area the mutual savings banks control over 70% of the total savings, and thus set the pattern for rates, the situation is reversed in California where commercial banks control more than 70% of total savings in the state and do not fear rate competition from savings and loan institutions as much as they might elsewhere in the country.

Accordingly, if California commercial banks feel that the profit margin on time or savings deposits is not sufficient, and that a lower rate would result in little deposit shrinkage—two conclusions we believe to be inescapable—a cut in the interest rates paid is not only a likely possibility but seems inevitable under the circumstances. If the interest rate were reduced back to the 2% level prevailing in 1956, significant earnings gains can result for California banks even in the face of lower gross earnings. Even assuming a decline of 5% in gross earnings as a result of the current recession, a decline that would be quite severe in view of the fact that gross earnings have not declined once in the post-war period, earnings gains of 7% to 17% are more than likely in selected California bank stocks should rates be reduced to the 2% level.

From this discussion, it seems clear that an attractive investment opportunity is being created at this time. The pendulum of investment interest, in our opinion, will shortly reverse itself and swing back to the presently depressed California banks, which still, after all, have an outstanding record of growth over the past decade and bright, long-term prospects. Accordingly, we would recommend purchases of such California bank stocks as Firstamerica Corporation, Bank of America, and Security First National Bank.

FIRSTAMERICA CORPORATION

Firstamerica represents the spun-off banking interests of Transamerica Corporation. Firstamerica is a bank holding company which, as of year-end 1957, had 23 majority-owned banks with 322 banking offices in 11 western states. The First Western Bank & Trust Company, 73% owned, with 97 banking offices in California, is the largest bank in the Firstamerica family, controlling approximately

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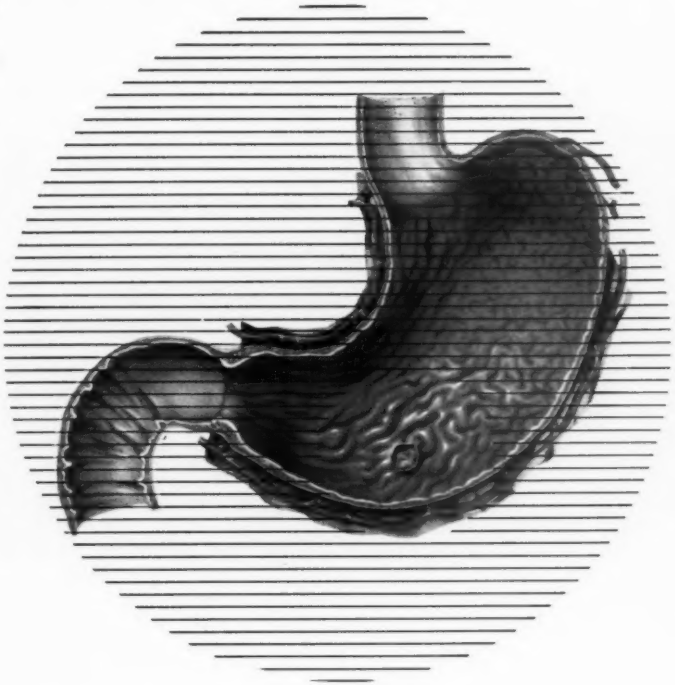


And AMPHOJEL—nonsystemic, nontoxic—provides time-proved fundamental therapy. It combines two aluminum hydroxide gels—one reactive, the other demulcent—for two specific purposes. The reactive gel promptly buffers gastric acidity. The demulcent gel promotes healing of denuded mucosa by forming a viscous, protective coagulum.

FUNDAMENTAL THERAPY IN PEPTIC ULCER

Wyeth
Philadelphia 1, Pa.

AMPHOJEL® double gel for diphasic action

Aluminum Hydroxide Gel, Wyeth

Firstamerica Corp.	
	Capitalization (June 5, 1958)
Price 17½	Common stock .....11,372,022 sh.
Indicated Dividend .....80¢	
Yield 4.6%	
Traded .....N.Y.S.E.	
1958 Price Range 18-15¼	

32% of deposits. Other important banks include the First National Bank of Portland, 58%-owned, with 76 banking offices; and the First National Bank of Arizona, Phoenix, 58%-owned, with 50 banking offices. The other 20 banks owned, while smaller in size—ranging from $215 million in deposits for the First National Bank of Nevada to $7 million for the Bank of Glacier County, Montana — are leading and important financial institutions in the areas they serve. The 11 western states served by Firstamerica have excellent long-term growth prospects.

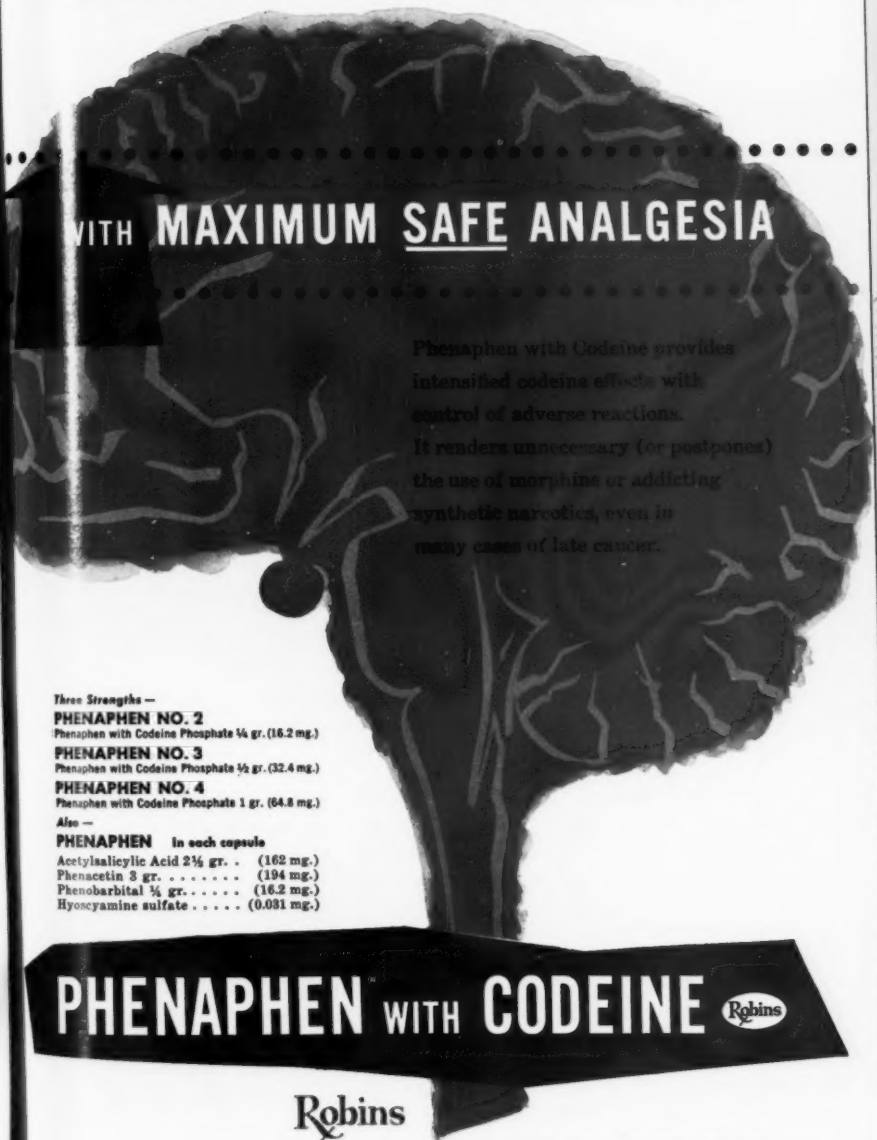
There are two important earnings results published by most banks. Banks report both "net operating income," which represents the results of banking operations. Banks also publish "net income," which includes both the results of banking operations and the profit and/or loss from the sale of securities owned by the bank. Since bond prices were generally low in 1957, most banks had and took losses on their bond portfolios. Thus, for banks in California as well as in all areas of the country last year, net operating income was generally higher than net income.

In 1957, Firstamerica's net income came to $1.19 per share. Net operating earnings, however, came to approximately $1.31 a share. This year, we expect net operating earnings to be equal to or even slightly higher than 1957 results. This excellent performance can be attributed to the wide diversification of Firstamerica's loans and discounts. Commercial and industrial loans account for only 27.3% of total loans, while real estate loans account for 43.5%—of which 26.8% are to some extent Government insured or guaranteed—and personal loans to individuals 21.5%. Real estate and individual loans not only make an important contribution of the earning power of the corporation, but also impart a great deal of stability due to the longer maturities.

In contrast to 1957, bond prices have risen sharply this year. Accordingly, it seems quite likely that Firstamerica, and other banks, will have profits to report from security transactions. With net operating earnings holding steady or even gaining, and with a profit replacing a loss in security transactions, a sharp gain is looked for in net income for the year.

Moreover, as of December 31, 1957, 43.4% of Firstamerica's controlled bank deposits of $2.9 billion were interest-bearing time deposits. Last year, interest payments as a percentage of gross income increased to 23% from 17.3% in 1956, and total operating expense ratio jumped 6.3 points to 72.5%. Thus, since other expense items as a percentage of gross income remained relatively steady, the increase in interest paid on deposits reduced net current operating earnings last year by more than 10%. Should the time deposit rate be cut,

Raise the Pain Threshold



WITH MAXIMUM SAFE ANALGESIA

Phenaphen with Codeine provides intensified codeine effects with control of adverse reactions. It renders unnecessary (or postpones) the use of morphine or addicting synthetic narcotics, even in many cases of late cancer.

Three Strengths —

PHENAPHEN NO. 2
Phenaphen with Codeine Phosphate ¼ gr. (16.2 mg.)

PHENAPHEN NO. 3
Phenaphen with Codeine Phosphate ½ gr. (32.4 mg.)

PHENAPHEN NO. 4
Phenaphen with Codeine Phosphate 1 gr. (64.8 mg.)

Also —

PHENAPHEN in each capsule

Acetylsalicylic Acid 2½ gr. . (162 mg.)
Phenacetin 3 gr. . . . . (194 mg.)
Phenobarbital ¼ gr. . . . . (16.2 mg.)
Hyoscyamine sulfate . . . . . (0.031 mg.)

PHENAPHEN WITH CODEINE Robins

Robins

A. H. ROBINS CO., INC., RICHMOND 20, VIRGINIA

Ethical Pharmaceuticals of Merit since 1878

Bank of America National Trust & Savings Assoc.			
		Capitalization (12/31/57)	
Price	38	Common stock	25,600,000 shs.
Dividend	$1.80		
Yield	4.7%		
Traded	O.T.C.		

a significant additional earnings gain can result over and above the above-mentioned gain.

Selling at little more than 13 times approximate 1957 net operating earnings, it is our opinion that Firstamerica Corp. shares at present prices offer good value and posses better-than-average growth prospects.

BANK OF AMERICA NATIONAL TRUST & SAVINGS ASSOCIATION

First organized in 1904 as the Bank of Italy, the Bank of America National Trust & Savings Association became a national bank in 1927. The present title was adopted in 1930 as a result of consolidation with the Bank of America of California. It is the largest publicly owned banking system in the world. There are 617 offices and 32 military banking facilities in California, and 9 branches and 9 military facilities overseas.

During 1957 California accounted for more than one-tenth of the nation's income. California's personal income rose to a new record high of $35 billion, growing at a 7% rate as compared with the national rate of 5% for the year. Nearly six million Californians were fully employed at the mid-year peak. Three out of every five adult residents were at work, with housewives, students and retired people finding profitable opportunities in industry. Notwithstanding economy measures in the defense program during the year, total wages paid to manufacturing workers increased by more than 10% to give the State's economy its greatest single boost.

One thousand new residents entered the state every day. This influx, combined with a natural population increase of 600 births every day, swelled California's population by almost 600,000 during the year to a new record high of 14.4 million.

The steady growth of the bank in recent years is shown in net operating earnings per share over the period. In 1952, net operating earnings were $2.37. These rose in 1953 to $2.66, held steady in 1954 at $2.64, then rose to $2.75 a share in 1955 and $2.89 a share in 1956. For the above-mentioned reasons, net operating earnings dipped slightly to $2.81 a share in 1957. Net income, however, was $2.59 a share in 1957.

Fully 50% of Bank of America's deposits as of year-end 1957 were interest-bearing time deposits, and the expense item interest paid soared from $73.6 million in 1956, or 19.9% of gross operating income, to $115 million, or 27.9% of gross operating income in 1957. The benefits to Bank of America of a reduction in interest rates paid on savings are thus obvious. We would recommend this stock for investors interested in long-term growth coupled with a fairly liberal yield.

25,000,000 courses of treatment— and NO "resistance" problems

*Conservative estimate based on combined use of all FURACIN preparations since 1945.

FURACIN®

In clinical use for more than 12 years and today the most widely prescribed single topical antibacterial, FURACIN—like other nitrofurans—remains effective against pathogens which have developed, or are prone to develop, resistance to other antibacterial agents. There has been no evidence that originally sensitive strains of staphylococci or other bacteria lose their susceptibility to FURACIN in any significant degree.

the wide-spectrum antibacterial exclusively for topical use ... in dosage forms for every topical need

Available as Soluble Dressing, Soluble Powder, or Solution. Also in Vaginal and Urethral Suppositories and in special formulations for eye, ear and nose.

one of the unique nitrofurans— products of Eaton research

Eaton Laboratories, Norwich, New York

The Nitrofurans

Security-First National Bank	
	Capitalization (12/31/57)
Price 48	Common stock .....5,880,000 shs.
Dividend $1.60	
Yield 3.3%	
Traded .....O.T.C.	

SECURITY - FIRST NATIONAL BANK

Security-First National Bank was formed in 1929 as a result of a consolidation of Security Trust & Savings Bank (organized 1889) and Los Angeles - First National Trust & Savings Bank (organized 1875 as a commercial bank). It is now the largest bank in Los Angeles and the second largest in California.

In 1956, the Farmers & Merchants National Bank was merged into Security-First, and during 1957, four other banks were merged—the Bank of Laguna Beach, Broadway State Bank, Citizens National Trust & Savings Bank of Riverside and Security Trust & Savings Bank of San Diego. There are now 205 offices maintained throughout central and southern California. The Pacific Southwest Realty Company, Citizens National Company, and Sectras Corporation, are wholly-owned subsidiaries.

Not even counting the benefit of various mergers, deposits and outstanding loans of Security-First have increased approximately 3½ times in the last 18 years. This outstanding growth record has stemmed in large part from the explosive expansion within the Bank's service area. Since 1940, population of this area has soared 116%, four times the rate for the nation as a whole.

Manufacturing employment in the same period has climbed from 244,500 to 914,900, an increase of 274% compared to a national gain of 55%. Similar vast gains have been scored by manufacturing payrolls, up 1,107%, personal income, up 549%, retail sales, up 498%, and construction up 800%.

The diversification of the industrial growth of the area shows up in the following breakdown of the area's major industries and occupations in terms of percentage of total employment as of 1956: wholesale and retail trade, 23%; service industries, 21%; aircraft and parts, 9%; construction, 7%; transportation and utilities, 6%; metal industries, 5%; finance, insurance and real estate, 5%; government, 4%; electronics, 3%; food, apparel and paper-publishing, each 2%; with the remaining 11% composed of numerous industries each accounting for less than 1% or less of employment. Per capital incomes in Southern California average approximately 25% higher than the national average.

Net operating earnings in 1957 came to $3.56 a share on a pro-forma basis, compared to $3.50 a share in 1956. Time deposits at the end of 1957 came to 38% of total deposits. Interest paid on deposits by Security-First National soared from $14.9 million to $25.9 million in 1957, rising from 14.3% of gross income to 20.8%. This reduced Security-First National's net operating profit margin from 19.7% to 17.7%.

Selling at a reasonable price-earnings ratio in relation to its dynamic prospects, the shares of Security-First National Bank appear attractive.◀

TAO *(Roerig)*

Oral triacetyloleandomycin, a medium spectrum antibiotic, with glucosamine to minimize interference of the antibiotic with the natural flora in the intestinal tract. *Indications:* For control of common pathogens (notably staphylococci) resistant to penicillin and erythromycin. *Dosage:* Adults, average dose is 250 mg. four times daily, 500 mg. four times daily may be given in more severe infections. Children, 8 months to 8 years, 30 mg./Kg of body weight in divided doses. *Supplied:* In bottles of 60, either 125 mg. or 250 mg. capsules.

Hydrocortisone-Neomycin Ointment *(Paul Maney)*

Each gram of ointment contains 3.5 mg. of neomycin as neomycin sulfate, and 10 mg. of hydrocortisone acetate. *Indications:* Topical, for the treatment of allergic and seborrheic dermatitis, neurodermatitis pruritus and vulvae, secondary infection in burns and pyogenic infections. Ophthalmic, inflammatory conditions of the anterior segment of the eye, allergies, trauma, burns, and following intra-ocular surgery. *Contraindications:* Ocular herpes simplex and ocular tuberculosis. *Dosage:* As directed by physician. *Supplied:* Ophthalmic or topical ointment in ⅛ ounce tubes.

Erythromid *(Abbott)*

Antibiotic with triple sulfas. Each Filmtab contains erythromycin stearate, equivalent to 75 mg. of the base, and 111 mg. each of sulfadiazine (sodium), sulfamerazine (sodium) and sulfamethazine. *Indications:* In the treatment of mixed infections caused by Gram-positive and Gram-negative bacteria sensitive to this combination of antibiotic and sulfonamides. In urinary and respiratory tract infections. *Dosage:* Adults, 2 or 3 Filmtabs 4 times daily. Children 60 pounds or more, 1 or 2 Filmtabs 4 times daily, children under 30 pounds, 1 Filmtab 4 times daily.

Meloxine Tablets *(Upjohn)*

Each tablet contains 10 mg. of methoxsalen. *Indications:* To enhance pigmentation and protect against sunburn, and to repigment vitiliginous areas. *Dosage:* As directed by physician. *Supplied:* In bottles of 28 tablets.

Fleet Enema, Pediatric Size *(Fleet)*

New size. Each disposable unit contains 2¼ fluid ounces. Each 100 cc. contains 16 gm. of sodium biphosphate and 6 gm. of sodium phosphate. *Supplied:* In single units.

when eating moves outdoors . . .

CREMOSUXIDINE®

SULFASUXIDINE® SUSPENSION WITH KAOLIN AND PECTIN

CONTROLS "SUMMER COMPLAINT"

For people at work or on vacation, "summer complaint" is an annoying hazard of warm weather. Changes in routine or in eating or drinking habits can cause diarrhea and ruin summer days.

CREMOSUXIDINE gives prompt control of seasonal diarrhea by providing antibacterial and antidiarrheal benefit. It detoxifies intestinal irritants and soothes inflamed mucosa.

Chocolate-mint flavored CREMOSUXIDINE is so pleasant to take too!

CREMOSUXIDINE and SULFASUXIDINE are trade-marks of Merck & Co., Inc.

MSD | MERCK SHARP & DOHME
DIVISION OF MERCK & CO., Inc., PHILADELPHIA 1, PA.

Sinaxar *(Armour Labs.)*

For treatment of conditions involving skeletal muscle spasm, through action on polysynaptic pathways in the central nervous system. Each tablet contains 200 mg. of styramate (2-hydroxy 2-phenylethyl carbamate). *Indications:* Fibrositis characterized by low back ache, muscle strains and pains, stiff neck, muscular rheumatism, muscular spasms found in frozen shoulder, arthritis, bursitis. *Dosage:* 1 or 2 tablets three times daily. *Supplied:* Bottles of 50 tablets.

Precalcin-D *(Walker)*

Pink and blue capsules. Blue capsules contain calcium lactate and pink capsules contain vitamins, minerals and bioflavonoids. *Indications:* Nutritional supplement for use during pregnancy and lactation. *Dosage:* One pink and 1 blue capsule daily. *Supplied:* In bottles of 60 and 300 capsules, half pink and half blue.

Enzactin Spray and Powder Pack *(Ayerst)*

Two new dosage forms. *Indications:* For treatment of athlete's foot and other superficial fungus infections. *Supplied:* Spray, 3 ounce containers in a propellant mixture. Powder Pack in a moisture-absorbent base, 1½ ounce puffer packages.

Compazine Spansule Capules 30 mg. *(S.K.F.)*

New dosage form. *Indications:* For mental and emotional disturbances. All-day or all-night therapy with one oral dose. *Supplied:* 30 mg. sustained-release capsules, bottles of 30 and 250 Spansules.

NOW...an advanced ACTH

SIGNIFICANTLY IMPROVED

CORTROPHIN®-ZINC

(Corticotropin-Alpha Zinc Hydroxide)

A unique electrolytic process* of manufacture gives a fine, easily resuspended aqueous suspension of Cortrophin-Zinc with these therapeutic advantages:

★ **VIRTUALLY PAINLESS** . . Unsurpassed patient acceptance.

★ **HIGH PURITY** . . . . . Virtually pure ACTH with fewer mg. of foreign protein per injection.

★ **RAPID ACTION** . . . . . New form stimulates peak adrenal output within two hours.

★ **LONG ACTION** . . . . . Provides ACTH activity for several days.

★ **ECONOMICAL** . . . . . Lower total ACTH dosage and fewer injections required.

Cortrophin-Zinc is indicated in the treatment of more than 100 diseases, including rheumatoid arthritis, bronchial asthma, allergies and hypersensitivities, bursitis, serum sickness, conjunctivitis and other eye diseases, ulcerative colitis, atopic dermatitis and other skin diseases.

★ **Ask your Organon representative or write for clinical and experimental reports substantiating these claims.**

SUPPLIED: 5-cc vials containing 40 and 20 U.S.P. units of corticotropin per cc; 1-cc ampuls containing 40 and 20 U.S.P. units of corticotropin, with sterile disposable syringes.

*Pat. Pending

Available in other countries as Cortrophine-Z.

Organon inc ORANGE, N.J.

Medrol 2 mg. Tablets *(Upjohn)*

New dosage. Anti-inflammatory steroid with high potency at low dosage. New 2 mg. tablet permits more exact dosage adjustment. *Indications:* Rheumatic, allergic, dermatologic, ocular and other conditions responsive to the anti-inflammatory corticosteroids. *Dosage:* Orally, under the supervision of the physician.

Pyribenzamine Compound With Privine *(Ciba)*

A disposable, plastic nebulizer containing 0.25% *Pyribenzamine* hydrochloride and 0.025% *Privine* hydrochloride in an aqueous solution adjusted to a pH of 5.2 to 6.0. *Indications:* For use in hay fever and other forms of allergic rhinitis. *Dosage:* One or 2 applications to each nostril every 4 to 6 hours. *Supplied:* Individual plastic nebulizers containing 15 ml. of solution.

Margel Deltabs *(Marvin R. Thompson)*

Combination of antacid ingredients with adsorbent charcoal in which each tablet inactivates 100 cc. of N/10 gastric acids. *Indications:* For relief of gastric hyperacidity. *Dosage:* One to 4 tablets ½ hour after meals. *Supplied:* In bottles containing 125 tablets and a pocket dispenser.

Sterane Intramuscular *(Pfizer)*

An aqueous normal saline suspension of prednisolone. Each cc. contains 25 mg. of the synthetic crystalline steroid for intramuscular use. *Indications:* For use in rheumatoid arthritis and other collagen diseases, neoplastic diseases, bronchial asthma, and inflammatory skin disorders such as atopic dermatitis. *Dosage:* For intramuscular injection under the supervision of the physician. *Supplied:* In 5 cc. rubber-stoppered vials.

Tetrex with T/S *(Bristol)*

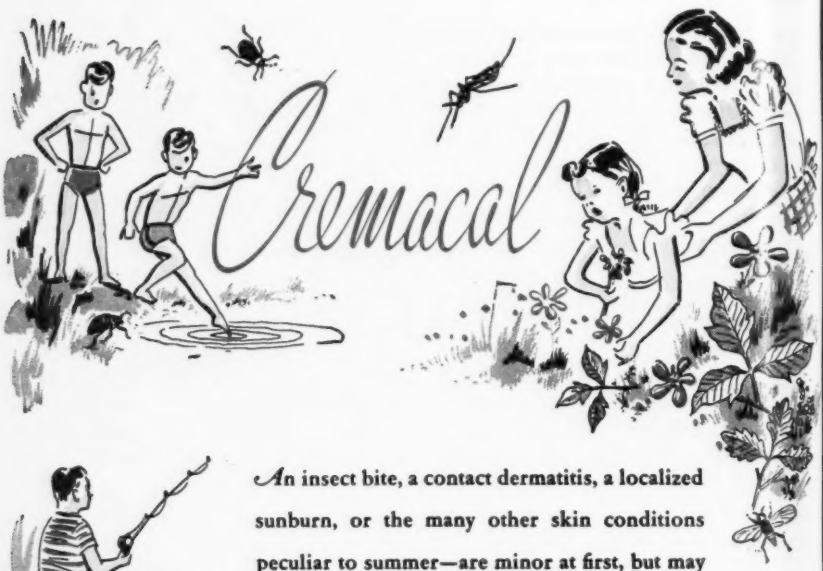
Each teaspoonful contains tetracycline equivalent to 125 mg. tetracycline hydrochloride activity, and 167 mg. each of sulfadiazine, sulfamerazine and sulfamethazine. *Indications:* Severe or mixed infections that do not respond to tetracycline alone. Shigella dysentery. *Dosage:* As directed by physician. *Supplied:* In bottles containing 2 fluid ounces.

Neohydrin with Vitamins *(Lakeside)*

New dosage form. Contains B vitamins and ascorbic acid in addition to the diuretic. *Indications:* For the management of edema and at the same time to protect the patient from nutritional deficiencies which often accompany low-sodium diets and diuresis. *Dosage:* As directed by physician. *Supplied:* Bottles of 50 tablets.

Gantrisin Cream *(Roche)*

New package. Now available with 18 disposable applicators. *Indications:* Cervicitis, vaginitis, vulvitis and related gynecological disorders. The pH is approximately 4.6 for acid reaction. *Dosage:* One half to 1 applicatorful twice daily, in the morning and upon retiring. *Supplied:* Each package contains a 3 ounce tube of cream and 18 disposable applicators.



An insect bite, a contact dermatitis, a localized sunburn, or the many other skin conditions peculiar to summer—are minor at first, but may become considerably aggravated by irritation from scratching or from contact with clothing.

CREMACAL affords protective action with cooling relief. It forms a tough protective film which resists scratching or irritation from clothing.

Although the CREMACAL film is tough and adherent, it can be easily rinsed off with plain water.

Calamine 10% . . . Benzocaine 1% . . . Phenol .5% . . . Menthol .25% in a special greaseless base.

HOBART LABORATORIES, INC.
Chicago 10, Ill. U.S.A.

briefs: MEDICAL

Correction of Bowel Function in Cardiovascular Disease

Many cardiac patients have a pronounced tendency toward constipation which may be dangerous in inviting complications and aggravation of the pathology. Dioctyl sodium sulfosuccinate was used for correction of bowel function in four groups of cardiac patients. The first group, 50 patients, had classic acute transmural myocardial infarction. The second group, 20 patients, had pulmonary emboli which resulted in pulmonary infarction. The third group, 18 patients, required bedrest for severe cardiac decompensation, and the fourth group of 15 patients were cardiacs of various types who were bedfast and in whom maintenance of normal bowel function was desirable to avoid exacerbation of the condition.

One 240 mg. capsule of the medication was given daily throughout the hospital stay with uniformly excellent results in all groups. There was no incidence of impaction, and straining on the bedpan was reduced. Where broad-spectrum antibiotics were also used, the consistency of the soft stool was not altered, even though such agents commonly cause a loose, watery evacuation. There was no interference with absorption of anticoagulant or other medication.

Dennison, A. D., Jr., *Am. J. Cardiol.*, 1:400,1958.

Unheralded Pulmonary Embolism

Pulmonary embolism accounts for 2 to 3 per cent of all hospital deaths. It is suspected when a patient has acute chest symptoms either postoperatively or after prolonged bed rest. It can occur in patients who appear to be fit, are active and have no signs of venous thrombosis, and in these patients diagnosis is difficult, as the clinical picture frequently resembles pneumonia.

Thrombosis of the calf veins may not produce pain or tenderness, may occur intra-abdominally. In one series, in 12 out of 70 fatal cases pulmonary emboli originated from sites other than the calf. Thus the absence of physical signs does not exclude the diagnosis of deep venous thrombosis.

Ten cases of pulmonary embolism are described. None of the patients had signs of peripheral venous thrombosis when first seen, and eight had been active until they developed chest symptoms. The patients treated with an anticoagulant recovered. Three patients died.

In nine of the cases, the clinical picture was that of recurrent attacks of pleurisy which did not respond to treatment with antibiotics. The sputum was blood-stained but not purulent—an important aid to diagnosis.

Cohen, H. & Daly, J. J., *Brit. M.J.*, 5055:1209-1212, 1957.

Nostyn Relieves Anxiety, Tension

A new agent, *Nostyn,* is chemically unrelated to any existing chemopsychotherapeutic agent, and appears to relieve anxiety and tension without producing mental depression or drowsiness. One hundred seventy-two patients complaining of one or more symptoms such as nervousness, restlessness, "inward tension," sense of insecurity, feeling of impending disaster, insomnia, respiratory difficulty and palpitation were given the medication. Many of the patients also had associated conditions including generalized arteriosclerosis, diabetes, the climacteric, obesity and heart disease. The period of observation varied from one to 33 weeks.

The drug acts rapidly, most patients experiencing calmative effects within a half hour. Many patients stated that their tension and agitation were relieved without making them feel "logey" or "doped-up." Although a few patients complained of drowsiness, especially at first, it was stressed that tension and anxiety may mask a state of fatigue which reveals itself when such symptoms are relieved. Thus, many patients whose anxiety and tension were relieved by the medication were able to enjoy normal sleep. Side effects were few and generally mild, and often disappeared during continued administration. There were no cumulative effects, signs of habituation or depression.

Bauer, H. G., et al., *New York J. Med.*, 58:520-526, 1958.

Pulmonary Histoplasmosis

Histoplasmosis, a generalized fungus disease that begins in the lungs, is world-wide in distribution, but the main endemic area comprises the Mississippi valley of the United States. The disease is as protean as tuberculosis in its clinical manifestations ranging from primary infection, which heals with few and mild symptoms, to cavitary pulmonary disease, to fatal dissemination.

In a young person who does not smoke and whose lesion shows calcification, a conservative approach is warranted. Evidence of growth, cavitation and strong suspicion of cancer are indications for wide resection.

Neither the clinical nor the x-ray picture is diagnostic of chronic pulmonary infection. In histoplasmosis, positive cultures from sputum are easily grown only from cavitary or endobronchial disease. Diagnosis depends on evaluation of skin test, complement-fixation data, and the character of calcifications in the chest and spleen.

In the endemic area among white children up to the age of 18, infection with *H. capsulatum* is at least eight times more common than that with *Mycobacterium tuberculosis.*

Serologic methods of diagnosis of histoplasmosis are not consistent. The diagnosis of active histoplasmosis is not made by positive serologic tests unless the patient has only recently come into an endemic area and there has been documented conversion of the histoplasmin skin test.

Baum, G. L. & Schwarz, J., *New England J. Med.*, 258:677-684,1958.

Some Aspects of Referred Pain

Normally, 6% saline will produce stinging pain around the site of injection. It may also produce deep aching pain, skin hyperalgesia and palpable muscle spasm, often bilateral, and all within the same somatomeral segment as the injection. These effects can be rapidly reduced by the injec-

tion of 2% procaine into the site of saline injection.

In patients with post-herpetic neuralgia or painful scars, 6% saline in the appropriate interspinous ligament will aggravate the pain and hyperalgesia. 2% procaine if given 2 to 5 minutes later into the same site will abolish this aggravation and reduce the level of spontaneous pain, sometimes abolishing it. Procaine given alone also will reduce spontaneous pain, but the effect is less marked and less lasting than that of saline and procaine. When a series of such combined injections is given there may be permanent reduction and very occasionally permanent abolition of spontaneous pain. In a patient with post-herpetic pain in the D3 and D4 segments on the left, and angina of effort referred to the left arm, intercostal nerve blocks of the herpetic area and procaine to the D3 and D4 interspinous ligaments each gave relief both of the herpetic pain and also of the angina of effort. Saline aggravated the post-herpetic pain but reduced the effort angina. Combined saline and procaine was more effective in relieving the herpetic pain, and repeated injections gave permanent improvement.

In patients with spinothalamic tract lesions referred pain from midline saline injection occurred only on the side with intact spinothalamic pathways. Referred sensation does occur to the other side, but it is a non-painful tingling.

The referred effects of saline and procaine are inconstant. With apparently the same technique they may vary in the same patient on different occasions; in other patients not occur at all. Nevertheless they have potential therapeutic applications.

Whitty, C. W. M., *Proc. Roy. Soc. Med.*, 51:159-160, 1958.

Parasternal Thoracic Mass

X-ray examination, postero-anterior and lateral, will determine the location of the mass. Careful fluoroscopic examination is important. If air is seen in the mass, it is a hernia. A barium enema will show whether or not the colon is involved in the mass or hernia. Failure of intraperitoneal air to enter into the mass does not rule out hernia or a lesion from the abdomen which is tenting the diaphragm upward, since there may be adhesions sealing off the upper abdomen.

Another important step in diagnosis is needle aspiration for fluid or tissue cells. The intimate contact of the mass with the sternum and anterior chest wall makes needle puncture easy and reasonably safe. The parasternal thoracic mass extends laterally and posteriorly from the sternum, blends with the heart shadow, and occurs more frequently on the right side of the chest. Pericardial cyst and parasternal or Morgagni hernia are the most frequent causes of such masses.

Brantigan, O. C., *Maryland M.J.*, 7:79-85,1958.

Broncholithiasis

Eight cases of broncholithiasis have been proved by surgery, bronchoscopy, or expectoration of a broncholith. This condition may be much more common than the number of cases recorded indicates. It should be included in the differential diagnosis of any case of bronchial obstruction, pulmonary suppuration, or hemorrhage with paroxysmal cough when the x-ray shows calcification. All eight cases were due to calcification of lymph nodes which perforated the bronchi. The x-ray findings may simulate those of the lung, cancer, lung abscess, bronchiectasis, recurrent pneumonitis, or fungal infection. Special x-ray techniques such as laminography, lateral and oblique films may be needed. Bronchograms and bronchoscopy are important in establishing the diagnosis. The etiologic agent may be found in the broncholiths. Early diagnosis and treatment are important since the broncholith can be removed and residual lung damage may be prevented. Conservative treatment is the choice, except where there is obstruction with irreversible damage to the lung. It is impossible to remove all the calcific deposits and those that remain may be the source of further symptoms.

Kress, M. B., et al., *Maryland M.J.*, 7:113-122,1958.

Abdominal Aortic Aneurysm

Elective resection of abdominal aneurysms and aortic homograft or prosthetic replacement can now be accomplished with low morbidity and mortality rates. Only those patients with renal insufficiency or severe cardiovascular or cerebrovascular disorders should be categorically denied surgical treatment. In view of the rapid progression of the majority of these lesions to fatal rupture, and in view of the current low mortality rate for elective surgical treatment, it is recommended that all patients with abdominal aortic aneurysms be examined with a view to operation as soon as the diagnosis is made. Once rupture has occurred, surgical intervention, although offering virtually the only hope for survival, increases fourfold in mortality rate.

Spear, H. C., et al., *J. Florida M.A.*, 44:1091-1097, 1958.

Recent Approaches to the Rapid Diagnosis of Infectious Diseases

Organisms for which a satisfactory specific phage is available may be identified within 24 hours. Viable organisms are required. Tissue culture is of particular value in reducing the time required to identify certain viruses, bacteria and protozoa.

The fluorescent antibody technique can be applied directly to specimens containing certain bacteria and parasites, making it possible to identify them within a period of one hour. This direct staining with fluorescein-tagged antibody is also applicable to viruses in tissue and tissue cultures.

Direct microscopic examination of organisms stained by the fluorescent antibody technique (bacteria, protozoa, etc.) and a combination of tissue culture, followed by staining with fluorescein-tagged antibodies (viruses) appear to be the most promising practical approaches to rapid identification of bacteria, fungi, parasites, and viruses. The time required varies from one hour to 24 hours.

Hogan, R. B., *The Recorder*, 22:16-24,1958.

Electroencephalography's Proper Role

The EEG varies normally from patient to patient, from time to time in the same patient, from one age to another, between the sleeping and the waking state, and depending upon whether the eyes are open or closed. Certain wave patterns are found most often in healthy persons, others most commonly with disease, five to 10 per cent of apparently normal people have "abnormal" EEG's. Patients may have epilepsy or other convulsive disorders, brain tumors, subdural hematomas or subarachnoid hemorrhages and have a normal EEG.

The EEG is often normal over an area from which the brain has been removed. It is commonly normal in patients who have had frontal lobotomy. The EEG usually does not indicate the presence within the brain of a cystic cavity that is not under tension.

On the other hand, the EEG may reveal valuable clues as to the presence of a supratentorial brain tumor. It is usually abnormal in cases of epilepsy, especially in childhood —petit mal seizures and psychomotor or temporal-lobe epilepsy. It is indispensable in localizing those cases of psychomotor epilepsy that require surgical treatment, although even here its testimony may be equivocal. It usually presents a picture of severe and diffuse abnormality in cases of encephalitis, and it may be of value in following the course of this disease.

Bucy, P. C., *J.A.M.A.*, 160:1232,1958.

Treatment of Feces Impaction

Twelve patients with impacted feces in whom enemas of water, mineral oil, or other substances had been used without success, were given enemas of either 5.0 gm. of *Caroid* or 0.13 gm. of crystalline papain in 300 cc. of a warm, aqueous solution of 1:5,000 *Zephiran Chloride*. In 10 of the 12 patients, a bowel movement followed the retention of one of these enemas for one hour. In debilitated or weak patients, the gluteal regions were brought together with strips of adhesive tape to prevent leakage. None of the patients had pain, tenesmus, tenderness, blood in the stools, or subsequent constipation or diarrhea.

Godfrey, G. C., & Miller, J. M., *U.S. Armed Forces M.J.*, 8:1131-1134,1957.

Carcinoma of the Breast Associated with Pregnancy

The survival of patients operated on for breast cancer during pregnancy or nursing is comparable to that of other cancer patients. Thirteen of 56 patients had mastectomies during pregnancy. All the patients with axillary spread were dead within four years. All of the local tumors occurred in the first two trimesters of pregnancy, while those with axillary spread occurred throughout pregnancy.

Of two patients who had further pregnancies, one with very advanced disease had a therapeutic abortion without appreciable effect on the course of disease, while the other, who was allowed to proceed to term, had no immediate untoward effects.

There were 17 women in whom a mass was noted during pregnancy, but treatment of the breast cancer was given post-partum. Two noted a lump during one pregnancy, but had no treatment until the end of a second pregnancy. Three patients had localized disease and 14 had metastases. Two of the three with localized disease survived five or more years, only one of 14 with metastatic disease.

Twelve patients operated on for breast cancer became pregnant later. Of the eight who had localized disease at the time of operation, nine survived for 10 or more years, two for more than 30 years. One had two children after mastectomy, and is without evidence of recurrence 35 years after operation. The few patients with axillary spread were dead within five years.

Therapeutic abortion cannot be clearly shown to have a favorable effect on the course of the disease.

White, T. T., *Northwest Med.*, 57:477-481,1958.

An Effective Method of Nebulizing Bronchodilator Aerosols

Relief of bronchospasm in bronchial asthma and pulmonary emphysema may be rapidly and effectively achieved by a new method of aerosol administration. The gas phase of dichloro-difluoromethane is used to propel the bronchodilator, contained in a separate nebulization chamber of a pocket size nebulizer. Propulsion of the aerosol is achieved by slight pressure of the thumb, permitting better coordination of the inspiration and the inhalation of the medication. The cooling effect on the upper respiratory tract mucous membrane produced by liquid phase chlorofluorocarbons is absent when the gas phase is utilized for nebulization.

Using this nebulizer a determination of the effects of a compound consisting of 0.4 isoproterenol and 2% phenylephrine, 0.5% isoproterenol and 2.25% racemic epinephrine on vital capacity, heart rate and blood pressure in patients with bronchospasm showed:

1. A mean rise in vital capacity varying from 29 to 36 per cent. The increase was not significantly different for all three bronchodilators.

2. The administration of doses of bronchodilator aerosols of the three drugs, producing relief of bronchospasm, caused no rise in systolic or diastolic pressure in normotensive or hypertensive patients with bronchopulmonary diseases immediately after or following prolonged use of the medication.

There was no tremulousness, tachycardia or palpitations when 0.4% isoproterenol and 2% phenylephrine was used by inhalation. There was an incidence of these side reactions of 16% and 14% for 0.5% isoproterenol and 2.25% for racemic epinephrine.

Beck, G. J., *Dis. Chest*, 33:6,1958.

Differential Diagnosis of Chest Pain

A carefully-taken history will almost always give important clues. Physical examination needs to be more complete in obscure cases, e.g., chest pain with evidence of phlebitis of the lower leg.

"Cracked" or greenstick fractured ribs may be caused by coughing or sneezing—the usual site, junction of the middle and anterior thirds of the fifth to the tenth ribs.

Chest wall pain due to rib, sternal, or spinal involvement by primary or metastatic cancer is often seen. Diagnosis is difficult until the cancer focus is large enough to be felt, to produce a pathologic fracture, or to be visualized on x-ray films. Knowledge that the patient has cancer alerts the physician to the possibility of such cause for chest pain.

Scalenus anticus syndrome and cervical rib pain occur most frequent in women. The pain is increased when there is downward traction on the arm.

Diagnostic aids include urinalysis (with Bence-Jones), blood counts, total protein and albumin-globulin ratio of the serum, various serologic tests, microscopic examination of the stained bone marrow, biopsy, needle aspiration, special x-ray methods, injection of sinuses with contrast substances, bacteriologic methods, demonstration of nearby or distant primary malignant tumors, and even the response to various therapeutic measures.

Monroe, J., *New York J. Med.*, 56:3347-3353,1958.

Intracranial Tumors

Of 157 patients with intracranial tumors, operative specimens were obtained from 134. Autopsy specimens were also obtained from 39 of these and from the remaining 23 patients.

Of the tumors, 71 were gliomas, 14 tumors of cranial nerves, 27 meningiomas, 18 pituitary and parapituitary tumors, three pineal tumors, and 12 miscellaneous. Secondary invasion of the brain from tumors in the area had occurred in the remaining 12 cases.

Of the 71 gliomas, 46 were astrocytomas and glioblastomas. Thirty-one of the patients with these tumors were males and 15 females between the ages of three and one-half and 61 years. In children 66 per cent of these tumors were infratentorial, while in adults there were only six infratentorial tumors and these were all in patients between the ages of 15 and 30 years. The posterior fossa tumors were all astrocytomas except for one astrocytomia *and* glioblastoma. Of the tumors of the cerebrum, the number of astrocytomas equalled that of glioblastomas. Of the deep-seated tumors, six were diagnosed as astrocytomas and three as glioblastomas. One of the miscellaneous tumors was a dermoid cyst, lined by stratified squamous epithelium, its wall containing many sebaceous glands.

An analysis of all the space-occupying lesions found at biopsy or autopsy showed that 19 per cent were due to cryptococcosis or cysticerocosis.

Gault, E. W., et al., *Australian & New Zealand J. Surg.*, 26:180-193,1957.

Surgical Treatment of Deafness

The basic lesion in the histopathology of otosclerosis is new bone formation in the vicinity of the stapes and oval window. This same process may occur elsewhere in the middle and inner ear. While efforts in the treatment of conductive deafness have been successful, nothing has been available for those individuals suffering with nerve deafness except hearing aids and lip reading.

Anyone who is suffering with conduction or mixed deafness, in whom the neural mechanism of the ear is functioning, is a potential candidate for the mobilization procedure and may obtain acceptable improvement in hearing acuity. A patient with no neural deafness component has a better chance for obtaining good hearing than one with a mixed type of deafness.

There is a choice between the fenestration procedure and mobilization of the stapes. The patient having a successful mobilization procedure will obtain better hearing than the one having a successful fenestration operation. In the latter there is a deliberate technical interruption of the con-

tinuity of the ossicles plus a limitation in motion of the drum membrane, thus there is a sacrifice of 20 to 25 decibels of hearing.

Fitz-Hugh, G. S., *Virginia M. Month.*, 85:251-252, 1958

Minor Gynecologic Operations on an Outpatient Basis

This service is feasible wherever operating suites are equipped with recovery rooms. In a period of one year, 1,150 gynecologic patients were anesthetized and allowed to go home on the same day—70% of the minor surgical procedures in the gynecologic department in that year. Of the 908 reported on in detail, indications were menorrhagia and/or metrorrhagia in 454, infertility in 215, postmenopausal bleeding in 56, incomplete abortion in 20, and miscellaneous in 163. Thiopental sodium supplemented with nitrous oxide and oxygen was the anesthetic used in 98% of the patients. The average time of anesthesia was 20 minutes. Curettages were performed on 803 patients, and a cervical biopsy was included in most of them. Cauterization of the cervix was also carried out in 119 patients. Malignancies were detected in 18 of the 908 patients.

There were 16 unplanned immediate admissions to the hospital after the operative procedure and 8 unplanned delayed admissions to the hospital from one to 42 days after operative procedure. Of 883 patients who attempted to have minor gynecologic operations as outpatients, 859 went home without complications within a few hours after the operation. This form of service is recommended to conserve hospital beds, nursing service, and the patient's time and money.

Vermeersen, J., et al., *Obst. & Gynec.*, 9:139-142,1957.

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*average of patients and indications seen in general practice. Source: independent research organization; name on request.

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Manganese (from Manganous Sulfate)	1 mg.
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briefs: THERAPEUTIC

Antileprosy Drug

An antileprosy drug, *Ciba 1906*, has been tested for three years among leprosy victims in Africa, with excellent results. The medication prevented residual skin scarring and disfigurement when used with other active medications, and was especially effective in treating children because its nontoxic nature allowed them the same dosage as adults. There are 600,000 registered lepers throughout the world, but the actual number of victims is more than ten times that figure. Although most prevalent in tropical countries, the disease exists as far north as Iceland. In the United States it is estimated that there are about 500 patients being treated at a colony near New Orleans, Louisiana.

Davel, T. F., et al., *Leprosy Rev.*, 29:25-44,1958.

Trial of a New Analgesic Combination

The results of previous pharmacologic and clinical studies indicate that ethoheptazine is a moderately potent analgesic, it causes little or no sedation, has no addiction liability, and few side effects.

The study included unselected, consecutive patients, 53 on the obstetric and 39 on the gynecologic clinic service. The age range was 15 to 72 years. Each *Zactrin* tablet contained 75 mg. of ethoheptazine citrate and 325 mg. (5 gm.) of aspirin.

For postpartum pain, two tablets were ordered after delivery, only when relief of pain was requested. For gynecologic patients subjected to major procedures, the first dose was on the third day; and, after minor procedures, at any time the patient experienced pain.

Analgesic effectiveness as rated by 53 obstetric and 39 gynecologic patients in a variety of painful conditions, was high in 50 to 100%. Number of doses administered to each patient was one to 12, over periods of one to seven days.

Side effects were minimal.

Roden, J. S. & Haugen, H. M., *Missouri Med.*, 55: 128-129,1958.

Control of Bleeding after Dermabrasion

One of the drawbacks of dermabrasion in removal of scars, pits and blemishes has been oozing during performance and in the postoperative period. *Adrenosem Salicylate* has been used widely in many procedures for control of capillary bleeding. In over 200 dermabrasions and other surgical procedures, a significant reduction in blood loss was observed after use of this drug. It is a valuable aid to plastic surgery in reducing blood loss and providing a clearer operative field.

Brown, W. S., *Northwest Med.*, 57:470-473,1958.

Developmental Arrest Due to Corticosteroid Intoxication in an Infant with Adrenocortical Virilism

A classic case of congenital adrenocortical virilism with tendency to sodium loss and dehydration is presented. Experience has indicated that such patients are adequately treated with 40 to 50 mg. of cortisone per square meter per day, in divided doses, by mouth. The requirement for sodium-retaining hormone appears to be adequately provided in the form of a 75 mg. DCA pellet implanted at six months intervals during infancy, without the addition of supplemental dietary sodium.

The effects of a large amount of cortisone, desoxycorticosterone acetate and sodium chloride on an infant with adrenocortical virilism are described. In addition to the classic manifestations of corticosteroid intoxication, he was found to be suffering from total developmental arrest with cessation of skull growth and neuromuscular maturation. These evidences of intoxication subsided rapidly after reduction of the dosages to minimal effective levels.

It is believed that this sort of difficulty can be avoided by the use of rate of statural growth, combined with occasional observations of skeletal maturation, as guides to cortisone dosage in infants and children with this disease.

Drescher, A. N., et al., *New England J. Med.*, 257: 1280-1281,1957.

Hematologic Findings in Normal Women

Red blood cell counts and hemoglobin determinations were done on 663 women, divided into three groups. The first group included 84 "normal" women, the second included 293 women who were normal with physiological variants, and the third group of 286 women were normal with gynecologic variants. The first group had a higher mean red blood cell count and hemoglobin level than the second group, as determined by statistical analysis using the "t" test. The values in the first group were also higher than in the second and third group considered together. However, the values in the first group alone were not significantly higher than in the third group alone. Values in the second group were lower than in each of the other two groups and also lower than in the other two groups considered together.

The currently accepted normal female figure for hemoglobin level is 14 gm. of hemoglobin per 100 cc. The figure for red blood cells is 4,800,000 cells per cubic millimeter.

In the determinations done on the three described groups, a total of 663 women, the mean or average red blood cell count was 4,370,000 per cubic millimeter, with a range between 3,810,000 and 5,030,000. The mean hemoglobin level was 12.55 gm. per 100 cc. with a range of 10.2 to 14.8 gm. It is concluded that the currently accepted "normal" values are set at too high a level.

Judy, H. E., et al., *J.A.M.A.*, 167:563-566,1958.

Treatment of Acne Vulgaris

A tetracycline lotion is recommended in the treatment of acne vulgaris. Good results were reported in 15 of 20 patients with moderately severe, and in 20 of 27 cases of severe acne. Best results were obtained in patients who presented pustular, papulopustular and cystic lesions.

Hollander, L., et al., *Am. Pract. & Digest Treat.*, 8:1602,1957.

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Effects of Trypsin Administered Intramuscularly in Ophthalmology

Sixty-three patients with various eye diseases characterized by inflammation and edema were given intramuscular injections of 2.5 mg. of trypsin in oil every 12 hours for two days and once a day thereafter until the edema or the inflammation had disappeared. In 15 patients with ocular trauma the edema was totally absorbed after 48 hours of treatment. Fair results were obtained in two patients with commotio retinae. Very good results were obtained in patients with uveitis. The hypopyon disappeared after three days of treatment in a 70 year old patient with hypopyon keratitis, and the inflammation of the cornea disappeared after six days of treatment. Poor results were obtained in patients with epidemic kerato-conjunctivitis.

It is believed that trypsin can be used instead of cortisone in patients with inflammation of the eye whenever cortisone has no effect or is contraindicated. Very good results were obtained in patients with retinal venous thrombosis if they received early treatment. Disappearance of the retinal alterations and complete return of the retinal function was obtained after 20 days of treatment in a 45 year old patient with thrombosis of the central vein of the retina. Once the occlusion has set in, the therapy has a beneficial effect on the absorption of the edema and of the hemorrhage, but has no effect on the pathogenetic mechanism of the occlusion. Trypsin therapy has no effect on patients with retinopathies due to diabetes or diseases of the kidney. The treatment was not interrupted because of complications due to therapy.

Gennaro, A. & Romagnoli, M. A., *Minerva med.*, 48:1519-1521,1957.

Prolonged Use of Estrogens and Androgens in Postmenopausal and Senile Osteoporosis

Osteoporosis is a common disease state of postmenopausal women that may produce severe and disabling back pain, for which estrogen and androgen therapy is effective, safe, and simple. The best-tolerated estrogen appears to be *Premarin* (conjugated estrogenic substances), in doses of 1.25 to 5 mg. daily in a cyclical fashion. Since more than 5 mg. of methyltestosterone daily often produces undesirable and sometimes irreversible masculinization, testosterone was added only in the senile, severely debilitated, or extremely osteoporotic patient. Senile men with osteoporosis were treated with 30 mg. of methyltestosterone daily by linguet, or buccal tablet. The development of gynecomastia and loss of libido and potentia in the man treated with significant amounts of estrogen often limits the use of estrogens. Estrogens and androgens are prone to cause salt and water retention, and edema in older patients. This can often be prevented or corrected with salt restrictions and diuretics. Examination is made before therapy and at regular intervals for breast, cervical, endometrial, and prostatic malignancy.

The prolonged administration of estrogens relieves the hot flashes of the menopause and often causes a striking return to stability, sleep patterns, and sense of energy.

Henneman, P. H. & Wallach, S., *Arch. Int. Med.*, 100:715-723,1957.

briefs: OBSTETRIC

Toxemia of Pregnancy: A New Treatment for Controlling Edema

The sudden post-menstrual diuresis has been compared with the diuresis of parturition. Pregnanediol secretion occurs after ovulation and stops one to four days before the flow, but persists in the urine if pregnancy occurs. Pregnanediol secretion reaches its peak several weeks before parturition and disappears 24 to 28 hours after delivery. Diminished excretion of estrogen and pregnanediol has been found to precede development of symptoms of preeclampsia and eclampsia. These facts suggested the treatment of edema of pregnancy with a combination of a new 8-bromotheophyllinate compound and pyrilamine maleate.

The preparation was given to 180 pregnant patients with existing or developing edema. All but 18 (10%) responded satisfactorily. Weight gain was arrested, blood pressure lowered, edema and albuminuria reduced or eliminated. None of the 162 showed any side-effects. None of the 18 who failed to improve responded to any other measure. All required bed rest, with low-salt, high-protein diets. Eclampsia developed in one woman who recovered following delivery of a stillborn infant. The drug appears to possess a specific antidiuretic hormone antagonism, which accounts for its effectiveness in both premenstrual tension and edema of pregnancy.

James, W. F. B., & Johnson, A. P., *Am. J. Obst. & Gynec.*, 74:1054-1058,1957.

Prevention of Mid-Pregnancy Abortions

Dilation of the lower uterine segment taking place prematurely in patients with incompetent internal os might explain the extrusion of the membranes through a patulous cervix. If this could be the explanation, why do the membranes not extrude at later phases of "normal" pregnancies? At term, x-rays of repaired cervices and internal ostia reveal sutures placed at the internal os to be at a level with the biparietal diameter of the baby's head.

All transverse low-segment incisions at cesarean sections were made inferior to the uppermost wire sutures placed previously. This graphically corroborates the origin of the lower uterine segment and bears out the statement of Danforth and Ivy that "a specific point of junction of lower and upper segments cannot be distinguished in the uterus up to the fifth lunar month of pregnancy." It does not explain the failure of the membranes to extrude at term. Perhaps the sphincter-action of the entire isthmus, including the histologic os, prevents this accident of mid-pregnancy.

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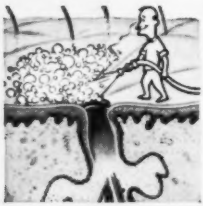

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The surgical procedure, as originated by Lash, is highly effective in allowing these patients to bear viable children.

McCall, J. O., Jr., *Northwest Med.*, 56:1438-1443, 1957.

Hemorrhagic Disease of the Newborn

During the past two years seven newborn infants with bleeding due to hemorrhagic disease have been seen. Each of the infants was delivered by a midwife, all but one normally. Six of these patients were found to have prolonged prothrombin time. None of the mothers had received oral vitamin K ante-partum, nor had either infant been given vitamin K.

Vitamin K is effective in controlling prolonged prothrombin time in the newborn infant. Practically all newborn nurseries use vitamin K to prevent bleeding in the newborn period. It may be given to the pregnant woman, a 1 mg. tablet daily during the last two weeks of pregnancy. If labor begins before such therapy, then 4.8 mg. intramuscularly every 24 hours during labor until delivery. Many believe that this therapy decreases the incidence of intracranial hemorrhage in the newborn. For newborns delivered at home, injection of 1 mg. menadione intramuscularly immediately following delivery is advocated.

A single dose of a water-soluble analogue equivalent to 1 mg. of synthetic vitamin K (menadione) is adequate to prevent hemorrhagic disease in the newborn. This would correspond to a dose of 3 mg. of menadiol sodium diphosphate (Synkavite sodium diphosphate, vitamin K analogue). It is unwise to exceed this dose level.

Beach, M. W., et al., *J. South Carolina M.A.*, 53: 455-458,1957.

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1. Levy, S., *J.A.M.A.*,153:1260,1953
2. Thompson L., Procter, R., *North Carolina M. J.*, 15:596,1954
3. Thompson, L., Procter, R., *Clin. Med.* 3:325,1956

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briefs: UROLOGIC

A Potent Uricosuric Agent

Zoxazolamine has been widely used for the past two years for decreasing spasm of skeletal muscle. Side effects are transitory and gastrointestinal side effects are usually avoided by administration of the drug with food.

Formerly used as a muscle relaxant, the drug has been found to have a potent uricosuric effect in doses of 750 mg. per day. During administration of this drug, an adequate urine volume and an alkaline urine are desirable to minimize the possibility of urate precipitation in the urinary tract. It is an effective uricosuric agent with rapid onset of action, comparing favorably with probenecid and salicylates. Its apparently low toxicity and additional property of reducing skeletal-muscle spasm may make it of great value in the treatment of chronic gout.

Reed, E. B., et al., *New England J. Med.*, 258:894-896,1958.

Urological Aspects of Lower Abdominal Pain

Thirty or 40 per cent of all pathological processes discovered in the upper urinary tract are caused by congenital abnormalities. Cystic kidneys, unilateral or bilateral, poly- or mono- are painful at times, and frequently bleed. Supernumerary kidneys may be the seat of pain. A horseshoe kidney is subject to intermittent obstruction, sepsis and stone formation with their symptoms. It should be considered in any case of undiagnosed lower-abdominal pain. A malrotated kidney may cause pain by pressing on the bowel, by pulling on a pedicle or by intermittent hydronephrosis. Congenital hydronephrosis is often found after a child has been examined because of nausea, vomiting and lassitude—the cause a non-functioning section of a double kidney. Aberrant vessels are notorious for causing intermittent or steady, colicky pain in the flank and radiating to the lower abdomen, or only in the lower abdomen, usually to one side. Ureterocele causes pain by vesical distention, back pressure, irritation and spasm. Congenital vesical diverticulum may cause severe lower-abdominal pain.

Woodward, A., *J. Iowa M. Soc.*, 48:7-11,1958.

Conservative Management of Ureteral Calculi Without Use of Hazardous Instruments

Of 237 proved ureteral stones in 200 men and 18 women, 186 stones were passed spontaneously without accident or complications; 38 were removed cystoscopically (33 on the first attempt and five on a second or later attempt); and 13 were removed by ureterolithotomy. Two of the five patients, after two or more attempts were made to remove the stones cys-


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toscopically, had attacks of pyelonephritis after the unsuccessful efforts, but there were no accidents. A total of 15 attacks of pyelonephritis occurred among those patients in whom cystoscopic efforts to remove stones of 0.6 to 1.3 cm. from the upper ureter failed. A ureteral perforation almost occurred in one of these patients. One patient, a chronic stone-former, died of renal insufficiency some months after the removal of a parathyroid adenoma. There were no other deaths.

In removing stones endoscopically, cystoscopic foreign-body forceps were used or a meatotomy was performed with the aid of cystoscopic scissors, but no rigid or metallic instruments were used beyond visual range. For stones above the meatus, various-size catheters were used. The results obtained show that ureteral stones can be adequately and safely handled without the use of hazardous instruments.

Gartman, E., *U.S. Armed Forces M.J.*, 8:313-320, 1957.

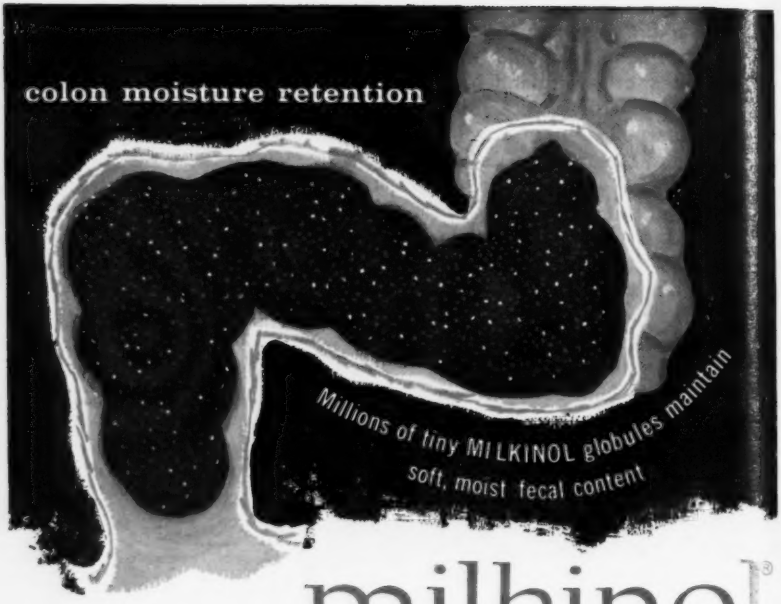
The Use of the Artificial Kidney in Acute Renal Failure

The artificial kidney has proved a valuable, and at times a life-saving adjunct to conservative management. Teschan et al., reporting on the Korean experience during 1952 state: "The mortality rate accompanying acute renal failure in military casualties in Korea was 80 to 90 per cent, similar to the mortality rate in World War II. After establishment of a Renal Insufficiency Center, and with the use of a Brigham-Kolff type artificial kidney, the mortality rate in 51 patients was 53 per cent."

Not all of the patients having dialysis responded favorably. However, improvement in some patients following dialysis was "of such degree that several patients requested another dialysis after the return of uremic symptoms during continued oliguria."

Still lacking is a clear demonstration of a significant improvement in mortality resulting from dialysis in cases of acute renal failure. The only generally accepted *contraindication* to dialysis is bleeding. Hyperkalemia and prolonged oliguria constitute the two paramount indications. The need for dialysis is frequently not recognized until an ambulance ride to a dialysis center is a serious threat to survival. All but the mildest cases should be cared for in institutions equipped to provide dialysis on short notice.

Bluemle, L. W., Jr., *Pennsylvania M.J.*, 60:1226-1227,1957.



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BOOK REVIEWS

Rehabilitation of the Cardiovascular Patient

by Paul Dudley White, M.D., New York University-Bellevue Medical Center, New York; Philip R. Lee, M.D., Palo Alto Clinic, Palo Alto, California; Bryan Williams, M.D., The University of Texas, Southwestern Medical School, Dallas. McGraw-Hill Book Company, Inc., The Blakiston Division, New York, Toronto & London. 1958. $7.00

This subject, of the very first importance, is presented by doctors of wide experience and sound judgment. The elaboration of the teaching that the cardiovascular patient should exercise systematically, up to the point at which nature tells him gently to desist, must contribute enormously to the happiness and the continued usefulness of this class of patients.

Our Nuclear Adventure: Its Possibilities and Perils

by D. G. Arnott, Philosophical Library, New York, N.Y. 1958. $6.00

Some doctors will wish to have this book to amplify their knowledge of the subject of nuclear power, and some may find in it a book to recommend to patients more than ordinarily concerned about developments in this field.

Ciba Foundation Symposium on the Chemistry and Biology of Mucopolysaccharides

Editors for the Ciba Foundation G. E. W. Wolstenholme, O.B.E., M.A., M.B., B. Ch. and Maeve O'Conner, B.A., with 48 illustrations. Little, Brown and Company, Boston, Mass. 1958. $8.50

This contribution in a new field will prove of special interest to pathologists, physiologists, and biochemists. However, there is enough on practical application to clinical problems to interest and prove useful to physicians and surgeons.

Old Doc

by O. H. Perry Pepper, M.D., J. B. Lippincott Company, Philadelphia. 1957. $3.75

The author tells us that "Old Doc is a composite of many physicians whom the author knew and admired for their simplicity and for their devotion to medicine and to humanity." All doctors who went to college early in the present century have known an "Old Doc," and will give Dr. Pepper's book a hearty welcome. Those few of the graduates of the last decade or two who will be interested in the subject will find much entertainment, and more than a little valuable information.

Current Surgical Management

A Book of Alternative Viewpoints on Controversial Surgical Problems, by John H. Mulholland, M.D., Editor-in-Chief, New York University College of Medicine; Edwin H. Ellison, M.D., Ohio State University College of Medicine; and Stanley R. Friesen, M.D., University of Kansas Medical Center; with contributions by 70 American Authorities. W. B. Saunders Company, Philadelphia, London. 1957. $10.00

A book made up of alternative opinions on controversial surgical problems. These alternative opinions, being held by surgeons equally able and equally eminent, cannot fail to serve an excellent purpose. Infallibility is expected of a surgeon only by those so ignorant as to be of no consequence. The passing of dogmatism in most fields of learning is a great encouragement.

The Chronically Ill

by Joseph Fox, Ph.D. Philosophical Library, Inc., New York N.Y. 1957. $3.95

There are chapters on "The Scope of Chronic Sickness, Caring for Long-term Disabilities, Taking up Life Again, Economic Aspects, Medical and Institutional Planning for Prolonged Illness," and several others. A hasty scanning reveals little that is not common knowledge among doctors of medicine.

Rheumatoid Arthritis

A Definition of the Disease and a Clinical Description Based on a Numerical Study of 293 Patients and Controls, by Charles L. Short, M.D., Walter Bauer, M.D. and William E. Reynolds, M.D. Harvard University Press, Cambridge, Mass. 1957. $7.00

The reader is oriented by an introduction and review of previous studies. Then follow diagnostic criteria for selection of patients, selection of controls and methods of analysis, and a scheme of presentation and definition of terms. From this point on, clinical description, cross-sectional and longitudinal, based on numerical studies of a large series of carefully observed patients, is presented in an attractive and informative fashion. It is said that the authors raise as many questions as they answer. Notwithstanding this, the doctor with such patients under his care will find in this book much that is helpful in their management.

Chemistry and Biology of Purines

editors for the Ciba Foundation, G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch. and Cecilia M. O'Connor, B.Sc. 124 illustrations and structural formulae. Little, Brown and Company, Boston. 1957. $9.00

The interest of doctors in general in this subject is in usefulness in treatment. It is said that "The effects of six-mercaptopurine therapy in human leukemia are well known," that this preparation differs from corticotropin, the steroid hormones and folic acid antagonists in its slow action, and that the doctor's satisfaction in the excellent health of patients in remission is offset by the knowledge that relapse is inevitable in acute leukemia. The statements with regard to chronic leukemia is little, if any, more encouraging.

General Diagnosis and Therapy of Skin Diseases: An Introduction to Dermatology for Students and Physicians

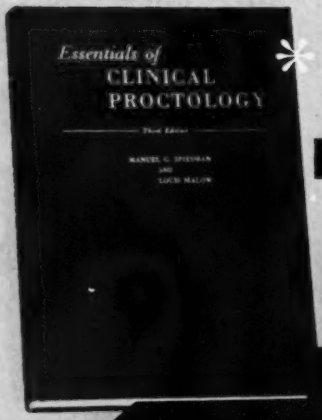
by Hermann Werner Siemens, M.D. University of Leiden, Holland; translated from the German edition by Kurt Wiener, M.D.. With 375 illustrations. The University of Chicago Press, Chicago, Ill. 1958. $10.00

It is said that the author makes a new approach to the teaching of dermatology, one that is broad and analytical, concentrating on the fundamentals and stressing the importance of scientific curiosity and intellectual discipline. Throughout, emphasis is placed on the value of the proved, old or new; no merit is assumed for any method or measure just because it is new. The illustrations are ample, without being so abundant and large as to suggest that the book is for those unable to read any writing other than picture-writing.

Physical Methods in Physiology

by W. T. Catton, M. Sc., King's College, Newcastle-upon-Tyne, Philosophical Library, Inc., New York, N.Y. 1957. $10.00

This book presents all that any practicing physician, all that most physiologists would need to know of the wide variety of experimental technics and theoretical treatments which are used in physiological investigation. It therefore covers a considerable part of the field of biophysics. It deals also with the physical treatment of physiological phenomena and includes as much of fundamental physiology as is necessary to make the technics meaningful.



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*Spiesman, M. G., and Malow, L.: Essentials of Clinical Proctology, Ed. 3, New York, Grune & Stratton, 1957.

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